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'Click chemistry' synthesis of a library of 1,2,3-triazole-substituted galactose derivatives and their evaluation against *Trypanosoma cruzi* and its cell surface *trans*-sialidase

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ABSTRACT

Trypanosoma cruzi trans-sialidase (TcTS) plays a key role in the recognition and invasion of host cells and in enabling the parasite to escape the human immune response. To explore this potential drug target, we have synthesized a small library of substrate analogues based on 1,4-disubstituted 1,2,3-triazole derivatives of galactose modified at either the C-1 or C-6 positions. This was achieved by coupling the appropriate azido-sugars with a panel of 23 structurally diverse terminal alkynes by using the copper(I)-catalyzed alkyne-azide cycloaddition (CuAAC) reaction, giving a library of 46 derivatives in good to excellent yield and with complete regioselectivity. The sugar triazoles showed weak inhibition towards TcTS-catalyzed hydrolysis of 2′-(4-methylumbelliferyl)-α-D-*N*-acetylneuraminic acid in vitro (<40% inhibition at 1 mM concentration); many of the compounds assessed proved to be acceptor substrates for the enzyme. Despite this modest inhibitory activity, in vitro trypanocidal activity assays against the trypomastigote form of *T. cruzi* Y strain revealed several compounds active in the low 100s of μM range. Further assessment of these compounds against cultured mouse spleen cells suggests a specific mode of anti-parasite action rather than a generic cytotoxic effect.

1. Introduction

Trypanosoma cruzi, the causative agent of Chagas' disease, is a protozoan parasite that must invade host cells in order to complete its life cycle. The parasite utilizes a cell surface *trans*-sialidase enzyme (TcTS) to transfer sialic acid from host cells to mucin-like glycoproteins in order to modify its carbohydrate coat so that it is not recognized by the human immune response and also to assist host cell invasion.[1,2] On both counts, inhibition of TcTS offers the potential for therapeutic intervention, since the enzyme represents a unique route by which the parasite acquires an essential sialic acid-containing coat. TcTS shares substantial sequence and structural homology with bacterial and viral sialidases.[3,4] However, while there are numerous nanomolar inhibitors of the latter that have made it into the clinic (anti-viral neuraminidase inhibitors, for instance),[5] there are very few respectable inhibitors (K_i <500 μM) of the parasite enzyme.[6,7]

In the search for new tools[8] with which to manipulate parasite glycosylation, potentially with therapeutic gain, we have been investigating the chemistry of the parasite cell surface mucin glycoproteins,[9] which are the natural acceptor substrates for TcTS.[10] In particular, the β-galactopyranoside residues (β-Gal*p*) on the mucin coat of the Y and CL-Brener strains of the parasite act as acceptors for TcTS-catalyzed transfer of sialic acid.[11,12] X-ray crystallography of co-complexes between the enzyme and substrates illustrates the contribution made by each hydroxyl group of galactose acceptors in binding to TcTS. Galactose positions 1 and 6 are not implicated in the binding process, whilst the galactose 3-OH is well positioned to interact with both the catalytic Asp59 and the anomeric carbon of the sialic acid donor substrate.[13] The selection of galactose positions 1 and 6 for modification was also based on the higher reactivity and ease of differentiation of these positions with respect to the other hydroxyl groups on the sugar ring. In addition, in a systematic assessment of TcTS acceptor substrate analogues, we have noted that modification at either the

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1 or 6 positions of galactose is accommodated by the enzyme.[14] A number of studies have also shown that TcTS has a great tolerance for β-galactoside substrates,[9,15–20] which prompted us to consider the exploration of the TcTS active site through the application of robust azide-alkyne 1,3-dipolar cycloaddition 'click chemistry' (CuAAC) based around modified carbohydrate templates.[21,22] Carbohydrates bearing a 1,2,3-triazole group prepared by 'click chemistry'[23] have been explored as potential inhibitors of glycosidases[24] and fucosyltransferases,[25] as well as for studying the substrate specificity of β-1,2-mannosyltransferases.[26] In addition, triazole-linked sialic acid derivatives have been investigated as inhibitors of influenza neuraminidases,[27,28] with replacement of the guanidino group of the commercially available anti-flu drug zanamivir by a 1,2,3-triazole group giving a similar EC_{50} to the parent drug.[27]

The current study focused on the chemical synthesis of a new class of 1,4-disubstituted 1,2,3-triazoles starting from galactose derivatives that bear an azide group at either the C-1 or C-6 positions. Coupling of such azides to a panel of 23 structurally diverse terminal alkynes using the copper(I)-catalyzed alkyne-azide cycloaddition (CuAAC) reaction[21–23] gave 46 disubstituted triazoles displaying a range of physicochemical properties. These compounds were assessed as TcTS inhibitors, as well as anti-trypanosomal agents; their cytotoxicity against a mammalian cell line is also reported.

2. Results and discussion

2.1. Synthesis of sugar azides

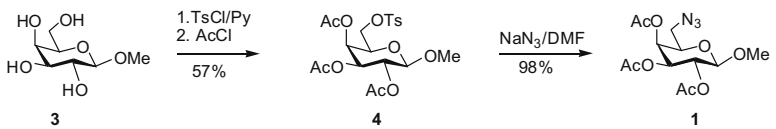
Although the derivatization of monosaccharides is very well explored, application of methods that are effective for one stereoisomer is not always predictable. The synthesis of protected 6-azido-6-deoxy-glycosides has previously been achieved by conventional procedures that involve either displacement of derivatives bearing a leaving group at C-6 (halogens or sulfonates) with inorganic azide[29,30] or directly from the free 6-OH compound with NaN_3 in the presence of PPh_3/CBr_4.[31] The latter has been successfully applied in the α-D-*gluco*- and α-D-*manno*-pyranoside series, while a β-D-glucopyranoside reacted to only a limited extent under the same conditions and a β-D-galactopyranoside was essentially unreactive. Although the synthesis of methyl 6-azido-6-deoxy-α-D-mannopyranoside has been described in high yield from the commercial methyl α-D-mannopyranoside by tosylation followed by azide displacement,[32–34] the same strategy applied to phenyl β-D-glucopyranosides gave the corresponding 6-azide derivative in only moderate yield.[35] On the other hand, Maunier[36] synthesized methyl 6-azido-6-deoxy-α-D-glucopyranoside in almost quantitative yield by substitution of the corresponding 6-chloro-6-deoxy derivative with sodium azide. Regarding galactopyranosides, to our knowledge only fully protected 6-azido-6-deoxy derivatives have been reported in the literature.[37] Even though two more protection/deprotection steps are required, the use of 1,2;3,4-di-*O*-isopropylidene-α-D-galactopyranose can provide the corresponding free 6-azido-6-deoxy sugar by treatment with mesyl chloride then NaN_3, followed by deprotection, in good yield (74%).[38] Driven by the need to prepare per-O-acetylated methyl 6-azido-6-deoxy-β-D-galactopyranoside (**1**), we adapted the route described for the α-D-*manno* series,[32] starting from methyl β-D-galactopyranoside, since use of di-*O*-isopropylidene galactose would require additional steps to cap the reducing terminus as a glycoside.

Preparation of 6-azido-galactoside **1** comprised 6-O-tosylation of methyl galactoside **3**, followed by tri-O-acetylation and displacement by azide, providing the desired product in 25% overall yield. The yield is compromised by a difficult separation of the unprotected sulfonate ester from the di-tosylate (O-3 and O-6) by-product. A significant improvement was achieved by performing a one pot tosylation/acetylation reaction, which afforded intermediate **4** in reasonable yield (56%) following chromatographic purification. The displacement of the 6-*O*-tosylate group of **4** with NaN_3 in DMF at 120 °C gave peracetylated methyl 6-azido-6-deoxy-β-D-galactopyranoside (**1**) in near quantitative yield (Scheme 1).

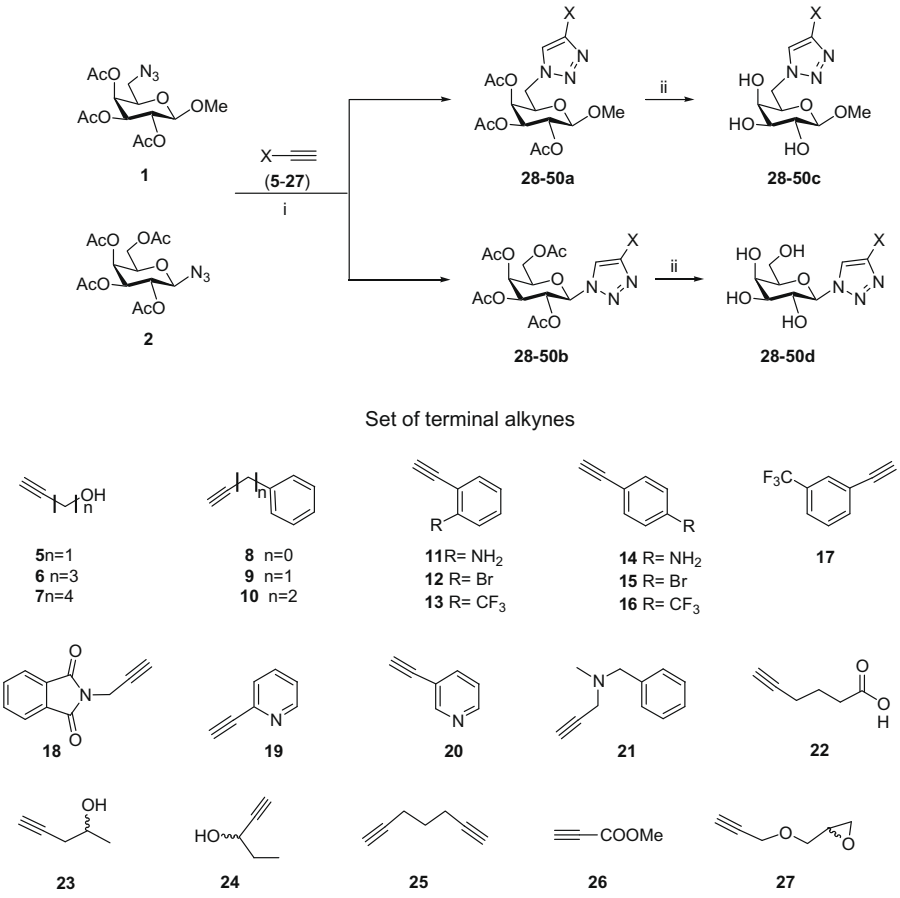
2.2. Triazole library synthesis

CuAAC reactions involving azido-galactoside **1** or the commercially available per-O-acetylated β-D-galactopyranosyl azide **2** were carried out with a diverse set of commercially available terminal alkynes, **5–27**, having different steric bulk, hydrogen-bonding and hydrophobic groups, linked to flexible and rigid side chains (Scheme 2). The 1,3-dipolar cycloaddition coupling was performed on a small scale (~0.13 mmol of azide) with a 10 mol % excess of the terminal alkynes in a sealed tube under microwave-assisted conditions. Copper sulfate (0.03 mM) and sodium ascorbate (0.1 mM) were used in the experiments for the in situ generation of Cu(I) catalyst. Typically, the reactions were conducted at 70 °C for 10 min in DMF (0.1 mL), with the progress of the reaction being monitored by TLC. After completion of the reaction, solvent was removed by co-evaporation with toluene. This approach using ester-protected sugar azides **1** and **2** allowed the separation of catalyst residues, as well as the removal of small impurities, by simple silica-gel filtration. Combinations of sugar azides **1** and **2** with 23 alkynes (**5–27**) afforded a diverse library of 46 derivatives **28a/b–50a/b** in excellent yields (70–100%), with two exceptions (compounds **48a** and **48b** were obtained in 33 and 44% yield, respectively), and with complete regioselectivity (only formation of the 1,4-disubstituted triazoles was noted, as judged by ^1H NMR spectroscopy—see below). Finally, removal of the acetate protecting groups with catalytic NaOMe in MeOH afforded the library of triazole galactosides (compounds **28c/d–50c/d**, Fig. 1) in near quantitative yield.

The majority of the 1,4-triazole-galactoside derivatives were obtained in one microwave cycle of 70 °C for 10 min. However, cycloaddition reactions involving terminal acetylenes **14**, **15**, **16**, **18** and **25** were more resistant to the initial coupling conditions and complete conversion was only achieved after 2 or 3 heating cycles of 70–100 °C for up to 30 min, which afforded products **37a/b**, **38a/b**, **39b**, **41b** and **48a/b**, respectively. The electron-withdrawing effects of functional groups at *para*-positions on the aromatic ring may influence the reactivity of the terminal alkyne, as illustrated by the presence of bromine in **15** and trifluoromethyl groups in **16**. Additionally, attempts at coupling 4-ethynyl pyridine with sugar azides **1** or **2** gave no product, even under more forcing conditions. Propargyl chloride and propiolic acid also proved unsuitable, with starting material remaining even after extended reaction, whilst reaction with propargyl amine resulted in notable



Scheme 1. Synthesis of methyl 6-azido-6-deoxy-β-D-galactopyranoside (**1**).



Scheme 2. Synthesis of a library of sugar triazoles obtained from dipolar cycloaddition reactions of galactose derivatives substituted with azide at C-6 (**1**) or C-1 (**2**) and a series of terminal alkynes (**5**–**27**). Reagents and conditions: (i) $CuSO_4$, Na ascorbate, DMF, microwave heating normally at 70 °C, 10 min; (ii) NaOMe, MeOH.

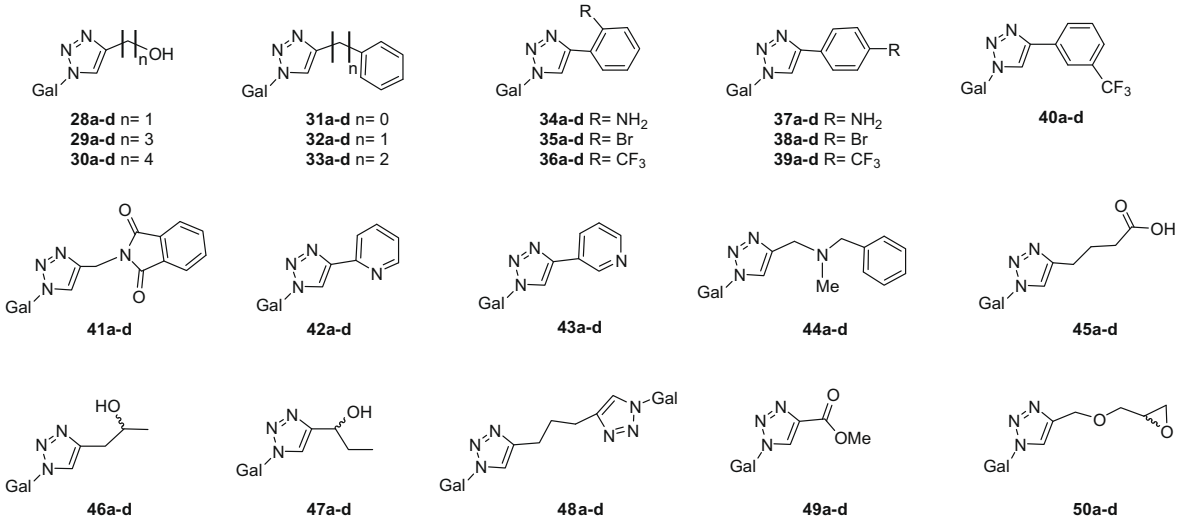


Figure 1. Library of sugar triazoles **28**–**50** (series **c** and **d**) obtained by deacetylation of adducts **28**–**50** (series **a** and **b**) synthesized from azides **1** or **2** and a diverse set of alkynes **5**–**27** by click chemistry approach.

product decomposition. Comparing the reactivity of 6-azide **1** and anomeric azide **2** under the CuAAC conditions with these more resistant acetylene derivatives, the reaction proceeded slower with azide **2** than azide **1** (Scheme 2). Furthermore, for the complete conversion of azide **2** to triazoles **37b** and **38b**, the reactions required heating (100 °C) for at least 15 min longer than the corresponding azide **1**. This is likely attributable to a combination of steric and electronic effects: elsewhere we have noted the impact of anomeric stereochemistry and glycoside bulk on the reactivity of glycosyl azides.[39] The condensation of the bis-alkyne **25** was also not straightforward, since the reaction provided the mono-triazole derivative, which was only converted to the dimer **48a/b** under forcing conditions and in lower yield.

The peracetylated 6-triazolyl-galactosides (library series **a**, Fig. 1) gave characteristic ^{1}H NMR signals, which showed the presence of one regioisomer.[23] For instance, the chemical shifts of the H-6 protons of both azido precursor **1** and products **28–50a**, were δ 3.1–3.5 (J ~12.0 Hz) and 4.3–4.6 (J ~14.0 Hz), respectively. For this library series, a minor influence of the triazole group was observed on the galactose H-5 signal, which has a chemical shift of δ 3.8 in the precursor **1** and approximately δ 4.0 in the **a** series library. Characteristic ^{1}H and ^{13}C signals of the triazole ring at 7.5 ppm (H-5′), 139.0 ppm (C-5′) and 148.0 ppm (C-4′), along with the triazole side chain, such as methylene signals of compounds **32a** and **32b**, respectively, at δ 4.11–4.02 and δ 4.21–4.10 ppm, were also observed. ^{1}H and ^{13}C NMR spectroscopy of galactosyl-triazoles **28–50b** showed chemical shifts of H-1 at δ 5.8–5.9 (J ~9.3 Hz), downfield compared to the precursor azide **2** at δ 4.6 (J ~8.6 Hz).

Furthermore, a modest downfield shift was observed for the galactose H-2 signal due to the influence of the triazole ring at C-1, changing from δ 5.1 ppm in azide **2** to approximately δ 5.5 ppm in the triazole products for **b** series. Regarding the heteroaromatic triazole ring in the **b** series, H-5′ was observed in the range δ 7.2–7.8 ppm, while C-5′ and C-4′ were at δ 138.0 ppm and 148.0 ppm, respectively, which is similar to the corresponding 6-triazolyl-galactoside **a** series. In summary, the structures and purity of each of the acetylated derivatives **28a**,**b**–**50a**,**b** were supported by spectroscopic data; following deacetylation the target deprotected compounds **28c**,**d**–**50c**,**d** were obtained in near quantitative yield.

2.3. Sugar triazoles as inhibitors of *Trypanosoma cruzi trans*-sialidase

Various methods for the determination of TcTS activity have been described.[40] Amongst them fluorimetric methods[40e] for assessment of the residual TcTS hydrolase activity are practical for screening purposes. Such assays, which are routinely used to assay microbial neuraminidases, rely on the residual hydrolase activity of TcTS, directly measuring the cleavage of 2′-(4-methylumbelliferyl)-α-D-*N*-acetylneuraminic acid (MuNANA) which releases fluorescent methylumbelliferone (Mu). Structural studies on TcTS-MuNANA complex and the ternary complex TcTS-lactose-DANA (DANA = 2,3-dehydro-2-deoxy-*N*-acetylneuraminic acid) show a common binding site for Mu and lactose,[41] where the latter may be viewed as either a product (where sialyllactose is used as a donor substrate) or an acceptor substrate. Kinetic analysis supporting a ping-pong mechanism for TcTS[42] shows no net effect on Mu production from MuNANA from the addition of lactose, which hides a compensating increase in K_m off-set by and increase in k_{cat} (i.e., addition of lactose results in no net change in k_{cat}/K_m). However, if a lactose (or galactose) derivative were to exhibit significantly different association or dissociation rates from TcTS, net inhibition of Mu release would be achieved.

With this in mind, and for ease of assay as highlighted above, a preliminary screen of the sugar triazole library (**28c**,**d**–**50c**,**d**) was conducted using TcTS-catalyzed hydrolysis of MuNANA. Results from this screen are summarized in Table 1, along with data for pyridoxal phosphate and DANA, which are reported to be weak TcTS inhibitors.[20] In general, compounds containing a triazole group at either the C-6 (**c** series) or C-1 (**d** series) position of galactose showed moderate to weak inhibition of TcTS at 0.5–1 mM concentration, with compound **32d** being the strongest TcTS inhibitor in these series (37% inhibition).

2.4. Sugar triazoles as acceptor substrates for *Trypanosoma cruzi trans*-sialidase

The mechanism of TcTS inhibition with galactose-based compounds may include direct competition with the donor substrate which might result in inhibition of *trans*-sialylation *per se*. Alternatively, a galactose-based compound might act as a TcTS substrate, competing with, and thereby inhibiting, the TcTS-catalyzed cleavage of MuNANA. Considering the promiscuity of TcTS towards substituted galactoside substrates,[14,15] additional assays were performed with the sugar triazole library to assess the potential of these compounds as *substrates* for TcTS-catalyzed *trans*-sialylation. These experiments were conducted by incubation of individual members of the triazole library with TcTS in the presence of MuNANA as a donor.[7] Although the TcTS enzyme used here is a recombinant His-tagged protein for ease of purification,[43] as noted elsewhere, crude cleared bacterial cell lysates are suitable for synthetic biotransformations.[9,10e,14,44,45] On an analytical scale, incubations showed near complete conversion of all members of the triazole library to the corresponding sialylated adducts within a few hours at room temperature, as judged by TLC and confirmed by ESI-MS analysis of the crude reaction mixtures. Data shown in Scheme 3 for triazoles **32c** and **32d** are representative of that obtained with either the C-6 substituted **c** series or C-1 substituted **d** series of sugar triazoles.

These biotransformation experiments show that while the sugar triazoles reported are indeed weak TcTS hydrolysis inhibitors they are more effective inhibitors than lactose and they are chemically competent substrates for the enzyme, so confirming their ability to bind to its active site.

2.5. In vitro trypanocidal activity and cytotoxicity towards mammalian cells

Before embarking on the optimization of the weak 'hits' obtained in the TcTS screen, and given the lack of any clear structure–activity relationship in the inhibition data, we first assessed the whole cell activity of the sugar triazole library. While TcTS is key to enabling parasite evasion of the human immune response, adhesion to and invasion of host cells,[1,2] it is not known to play a role in parasite survival in culture. Any trypanocidal activity from the sugar triazole library might therefore reasonably be interpreted as being TcTS-independent. In order to deconvolute general cytotoxicity from parasite-specific cell kill, the library was also screened against cultured mammalian cells.

2.5.1. Trypanocidal activity

The trypanocidal activity[46] of the entire sugar triazole library (**28c**,**d**–**50c**,**d**) was evaluated against the host infective trypomastigote form of *T. cruzi* Y strain using benznidazole (*N*-benzyl-2-nitro-1-imidazolacetamide), the current frontline drug used to treat Chagas disease as a control.[47] Data for the most active compounds are reported in Figure 2. Whilst many of the compounds displayed rather limited or no trypanocidal activity after 24 h at the tested concentrations, compounds **37d**, **39c**, **44c** and **48c**,**d**, with activities in the low 100s of μM range (approx 75 μg/mL), represent potential leads for further exploration. It is notable that **37d** and **44c** both have amine substituents attached to the triazole ring, whilst **48c** and **48d** contain two sugar units. The most active in vitro TcTS

Table 1
TcTS inhibition by sugar triazoles

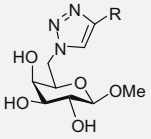
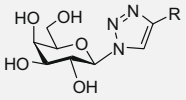
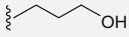
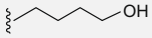
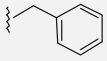
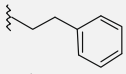
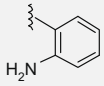
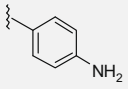
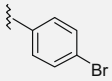
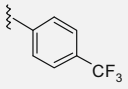
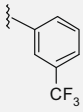
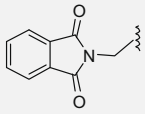
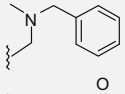
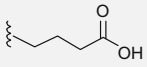
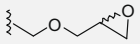
R	Compound 	% Inhibition at 1 mM[a,b]	Compound 	% Inhibition at 1 mM
	**28c**	28	**28d**	11
	**29c**	24	**29d**	27
	**30c**	27	**30d**	26
	**31c**	14	**31d**	15
	**32c**	29	**32d**	37
	**33c**	14	**33d**	16
	**34c**	24	**34d**	30
	**35c**	29	**35d**	33
	**36d**	11	**36d**	14
	**37c**	34	**37d**	19
	**38c**	3[c]	**38d**	Ni[c]
	**39c**	10[c]	**39d**	9[c]
	**40c**	3	**40d**	31
	**41c**	11[c]	**41d**	25
	**42c**	14	**42d**	13
	**43c**	20	**43d**	15[c]
	**44c**	17	**44d**	22
	**45c**	Ni	**45d**	10
	**46c**	10	**46d**	14
	**47c**	29	**47d**	13
	**48c**	16	**48d**	8
	**49c**	30	**49d**	28

Table 1 (*continued*)

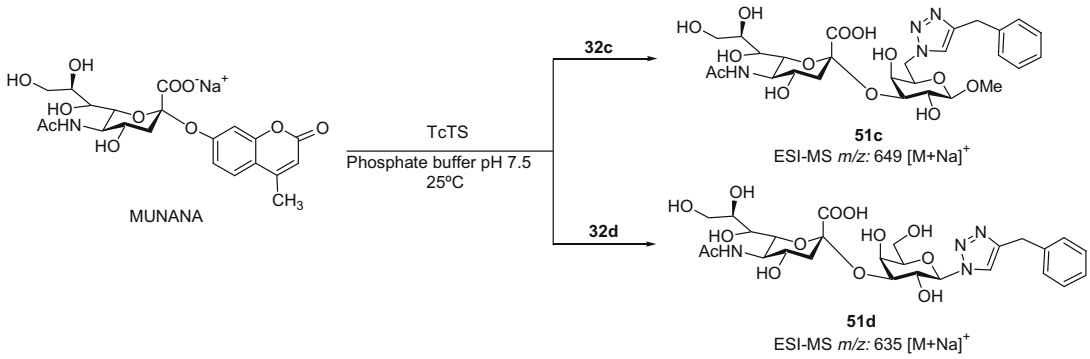
R	Compound	% Inhibition at 1 mM[a,b]	Compound	% Inhibition at 1 mM
	**50c**	25	**50d**	27
Pyridoxal phosphate		65		
DANA		33		

Ni: no inhibition.

[a] All data reported are accurate to ±5%.

[b] At 1 mM concentration, lactose shows no inhibition in this assay.

[c] Samples dissolved in H_2O containing 0.6% of DMSO and tested at 0.5 mM.



Scheme 3. Sialic acid transfer reactions catalyzed by TcTS using MuNANA as donor substrate and representative triazole-sugar acceptors **32c** and **32d**, to provide sialyl products **51c** and **51d**, respectively.

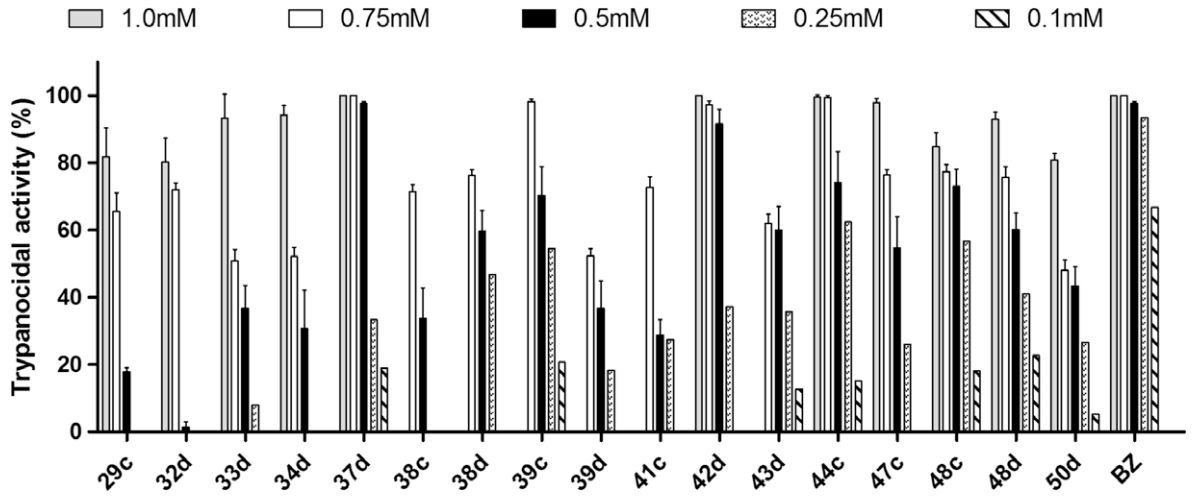


Figure 2. Trypanocidal activity of the **c** and **d** series sugar triazoles evaluated against trypomastigote forms of *T. cruzi* Y strain. BZ is the benznidazole control. For compounds **38c**, **38d**, **39c**, **39d**, **41c** and **43d** the maximum tested concentration was 0.75 mM due to their lower aqueous solubility, which required the addition of DMSO (0.6%).

inhibitor, **32d**, was not particularly active against the parasite (50% parasite cell kill in the high 100s of μM range) whilst whole parasite activities are evident at concentrations well below the level of in vitro TcTS inhibition for compounds **37d**, **39c**, **44c** and **48c**,**d**.

2.5.2. Mammalian cell toxicity

Moving on to mammalian cell toxicity, the trypanosome-active compounds highlighted in Figure 2 were screened against cultured mouse spleen cells;[48] data are shown in Figure 3. In this case, compounds **32d**, **38d**, **39c** and **43d** showed 50% mouse cell kill in the 50–100 μM range. Evidently mammalian cell toxicity does not directly mirror anti-parasite activity.

2.5.3. Comparative toxicity

Further analysis of Figures 2 and 3 identifies compounds that are toxic to the parasite but not to mouse cells (e.g., **29c**, **34d**, **37d**, **42d**, **44c**, **47c**, **48c**, **50d**), some that are much more toxic to mouse cells than to the parasites (e.g., **32d**, **38d**), and some that are toxic to both (e.g., **33d**, **38c**, **39c**, **39d**, **43d**, **48d**). There is no clear correlation between general compound structure (i.e., **c** or **d** series, 6- vs 1-position attachment of galactose to the triazole) and

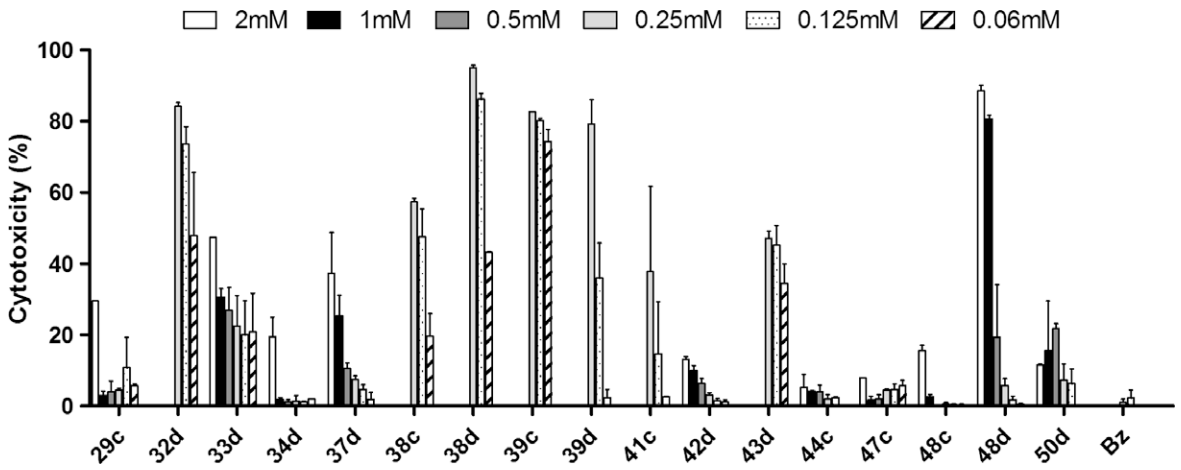


Figure 3. Percentage cell death caused by the **c** and **d** series sugar triazoles evaluated against cultured mouse spleen cells. BZ is benznidazole. For compounds **32d**, **38c**, **38d**, **39c**, **39d**, **41c** and **43d** the maximum tested concentration was 0.25 mM.

cell selectivity, but anti-mammalian cell activity is strongest for triazoles with hydrophobic substituents whilst anti-trypanosomal activity shows no such preference for triazole substituent.

3. Conclusions

In summary, a library of 46 sugar 1,2,3-triazoles was synthesized using copper(I)-catalyzed alkyne-azide cycloaddition (CuAAC) 'click chemistry' from galactose derivatives containing either a C6- or C1-azide group (compounds **1** and **2**, respectively). In general, these compounds proved to be moderate to weak TcTS inhibitors in vitro (<40% inhibition at 1 mM concentration), while all compounds evaluated showed the ability to act as acceptor substrates for TcTS-catalyzed *trans*-sialylation. Unexpectedly, some of the sugar triazoles showed trypanocidal activity in the low 100s of μM range against cultured trypomastigote forms of *T. cruzi* Y strain. These whole parasite activities are evident at concentrations well below the level of in vitro TcTS inhibition by the compounds concerned, indicative of a non-TcTS related mode of action at the cellular level. Assessment of the most active TcTS inhibitors as cytotoxic agents against mammalian cells established that some such compounds are toxic, but there is little direct correlation between anti-parasite activity and mammalian cell toxicity. Taken together, these data suggest that at least some sugar triazoles are not generic cytotoxic agent, but are capable of selectively affecting the parasite. *N*-Methyl benzylamine derivative **44c**, in particular, stands out as a candidate for further work (50% parasite kill at ~200 μM; <<10% mouse cell kill at 1 mM). Further studies to elucidate the mode of action of such sugar triazoles are clearly called for.

4. Experimental section

4.1. General methods

All chemicals were purchased as reagent grade and used without further purification. Solvents were dried according to standard methods.[49] 2,3,4,6-Tetra-*O*-acetyl-β-D-galactopyranosyl azide **2** was purchased from Carbosynth and MuNANA [2′-(4-methylumbelliferyl)-α-D-*N*-acetylneuramic acid sodium salt] was purchased from Toronto Research Chemicals Inc. Alkynes were purchased from Sigma–Aldrich. Benznidazole (*N*-benzyl-2-nitro-1-imidazolacetamide), used as positive control in the trypanocidal assays, was purchased from Roche. Reactions were monitored by thin layer chromatography (TLC) on 0.25 mm pre-coated silica gel plates (Whatman, AL SIL G/UV, aluminium backing) with the indicated eluents. Compounds were visualized under UV light (254 nm) and/or dipping in ethanol-sulfuric acid (95:5, v/v) or orcinol (2%) in aqueous sulfuric acid (10%), followed by heating the plate for a few minutes. Column chromatography was performed on silica gel 60 (Fluorochem, 35–70 mesh) or on a Biotage Horizon High-Performance FLASH Chromatography system using 12 mm or 25 mm flash cartridges with the eluents indicated. The microwave-assisted reactions were carried out in a Biotage Initiator System, using sealed tubes. All the fluorescence measurements were performed on a Synergy HT Multi-Mode Microplate Reader, using Gen5 software. Nuclear magnetic resonance spectra were recorded on a JEOL Lambda 400 MHz. ^{1}H NMR spectra recorded at 400 MHz were referenced to δ_H 7.27 for $CDCl_3$, δ_H 3.35 for CD_3OD, δ_H 4.63 ppm for D_2O, and ^{13}C NMR spectra recorded at 100 MHz and were referenced to δ_C 77.0 for $CDCl_3$ and δ_C 49.15 for CD_3OD. Assignments were made with the aid of HSQC and COSY experiments. Optical rotations were measured at ambient temperature on a Perkin–Elmer model 341 polarimeter using a sodium lamp. Accurate mass electrospray ionization mass spectra ESI-MS and ESI-HRMS were obtained from the John Innes Centre metabolite analysis service on a Thermo Finningan DecaXP^{plus} using positive and negative ionization modes, and Thermofisher LTQ Orbitrap XL mass spectrometers, respectively.

4.2. Methyl 2,3,4-tri-*O*-acetyl-6-*O*-*p*-toluenesulfonyl-β-D-galactopyranoside (4)

Methyl β-D-galactopyranoside **3** (1.0 g, 5.15 mmol) was dissolved in dry pyridine (12 mL) and cooled to 0 °C. Tosyl chloride (2.82 g, 15.0 mmol) was slowly added and the reaction mixture was stirred overnight at room temperature. Acetic anhydride (13 mL) was added subsequently and the mixture was stirred for 12 h. The mixture was concentrated by co-evaporation with toluene, diluted with DCM and the organic layer was washed with 1 M HCl, satd $NaHCO_3$ solution, dried ($MgSO_4$) and concentrated under reduced pressure. The crude product was purified by flash chromatography (EtOAc/Tol, 15–30%) to give compound **5** (1.37 g, 56%); mp = 47–50 °C; $[\alpha]_D^{25}$ −8.7 (*c* 1.0 $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz), δ (ppm): 7.77 (2H, d, *J* 8.2 Hz, Ar); 7.35 (2H, d, *J* 8.2 Hz, Ar); 5.36 (1H, dd, $J_{3,4}$ 3.3 Hz, $J_{4,5}$ 1.0 Hz, H-4); 5.14 (1H, dd, $J_{1,2}$ 7.8 Hz, $J_{2,3}$ 10.4 Hz, H-2); 4.98 (1H, dd, $J_{2,3}$ 10.4 Hz, $J_{3,4}$ 3.3 Hz, H-3); 4.36 (1H, d, $J_{1,2}$ 7.8 Hz, H-1); 4.13 (1H, dd, $J_{5,6'}$ 6.6 Hz, $J_{6,6'}$ 10.0 Hz, H-6′); 4.01 (1H, dd, $J_{5,6}$ 6.1 Hz, $J_{6,6'}$ 10.0 Hz, H-6); 3.94 (1H, dd, $J_{4,5}$ 1.0 Hz, $J_{5,6} = J_{5,6'}$ 6.4 Hz, H-5); 3.48 (3H, s, OMe); 2.46 (3H, s, CH_3Ar); 2.05, 2.03, 1.96 (9H, 3s, 3 × CH_3). ^{13}C NMR ($CDCl_3$, 100 MHz), δ (ppm): 169.8, 169.3 ($COCH_3$); 145.2

(C-Ar); 129.8, 127.9 (CH-Ar); 101.8 (C-1); 70.5 (C-5 or C-3); 70.4 (C-3 or C-5); 68.4 (C-2); 66.9 (C-4); 66.4 (C-6); 56.9 (OCH_3); 21.5 (CH_3Ar); 20.6–20.3 ($COCH_3$). IR (KBr) ν_{max}: 2941.2; 1755.1; 1367.4; 1220.9; 1078.1 cm^{-1}. ESI-MS *m/z*, calcd for $C_{20}H_{26}O_{11}S$ $[M+Na]^+$ 497.1, found 497.0.

4.3. Methyl 2,3,4-tri-*O*-acetyl-6-azido-6-deoxy-β-D-galactopyranoside (1)

A suspension of compound **4** (0.78 g, 1.65 mmol) in DMF (25 mL) containing sodium azide (1.63 g, 25.1 mmol) was heated at 120–130 °C for approx. 6 h. The solution was allowed to cool, diluted with water (30 mL) and extracted with DCM. The organic extract was washed with water, sat $NaHCO_3$ solution and water, dried ($MgSO_4$) and concentrated under reduced pressure to give compound **1** as a crystalline solid (0.56 g, 1.62 mmol, 98%); mp = 103–104 °C; $[\alpha]_D^{25}$ −15.0 (*c* 1.0 $CHCl_3$); ^1H NMR ($CDCl_3$, 400 MHz), δ (ppm): 5.34 (1H, dd, $J_{3,4}$ 3.4 Hz, $J_{4,5}$ 1.0 Hz, H-4); 5.20 (1H, dd, $J_{1,2}$ 7.8 Hz, $J_{2,3}$ 10.5 Hz, H-2); 5.03 (1H, dd, $J_{3,4}$ 3.4 Hz, $J_{2,3}$ 10.5 Hz, H-3); 4.4 (1H, d, $J_{1,2}$ 7.8 Hz, H-1); 3.86 (1H, ddd, $J_{4,5}$ 1.0 Hz, $J_{5,6}$ 4.0 Hz, $J_{5,6'}$8.4 Hz, H-5); 3.56 (1H, dd, $J_{5,6'}$ 8.4 Hz, $J_{6,6'}$ 13.0 Hz, H-6′); 3.55 (3H, s, OMe); 3.13 (1H, dd, $J_{5,6}$ 4.0 Hz, $J_{6,6'}$ 13.0 Hz, H-6); 2.16, 2.08, 1.91 (9H, 3s, 3 × CH_3). ^{13}C NMR ($CDCl_3$, 100 MHz), δ (ppm): 170.2, 170.0, 169.4 ($COCH_3$); 102.0 (C-1); 72.9 (C-5); 70.8 (C-3); 68.7 (C-2); 68.0 (C-4); 57.0 (OCH_3); 50.5 (C-6); 20.7, 20.5, 20.4 ($COCH_3$). IR (KBr) ν_{max}: 2941.2; 2100.3; 1747.4; 1244.0; 1047.3 cm^{-1}. ESI-MS *m/z*, calcd for $C_{13}H_{19}N_3O_8$ $[M+Na]^+$ 368.1, found 368.0. ESI-HRMS $[M+Na]^+$ calcd 368.10644, found 368.10693.

4.4. Synthesis of 1,2,3-triazole-modified galactosides by CuAAC click reaction

4.4.1. General procedure

Sugar derivative **1** or **2** containing azide group at C-6 or C-1 (0.13 mM), respectively, was dissolved in DMF (0.1 mL, solution 0.5–1.0 M) in a microwave flask (0.2 mL) equipped with a stirring bar. After dissolution, one of the acetylene derivatives **5–27** (0.15 mM, 1.1 equiv) was added. Then, sodium ascorbate (0.1 equiv) and $CuSO_4$ (0.03 equiv) were added and the tube was sealed. The mixture was stirred for 25 s and heated for 10 min at 70 °C (18 W) in the microwave, unless stated otherwise. The reaction was followed by TLC and after completion the reaction mixture was partitioned between H_2O and EtOAc, the aqueous phase was extracted with EtOAc (3–5 times depending on the solubility of the specific compound). The organic phase was dried over $MgSO_4$, filtered, concentrated and the residual solvent was finally co-evaporated with toluene. The peracetylated product (a compound of series **a** or **b**) was fully characterized prior the deprotection. The acetate was dissolved in methanol (1.0 mL) and sodium methoxide (1.0 M in methanol) was added until pH 9.0 was achieved. After stirring for 1 h at room temperature, the mixture was neutralized with Amberlite-IRA-400 (H^+), filtered and concentrated in vacuo. The resulting product (a compound of series **c** or **d**) was obtained in quantitative yield, not further purified and characterized by ESI-MS only. These data are shown in Sections 4.4.2–4.4.46 together with complete characterization data for acetylated precursors (compounds of series **a** or **b**).

4.4.2. [1-(Methyl 6-deoxy-β-D-galactopyranosid-6-yl)-1*H*-1,2,3-triazol-4-yl]-methanol (28c)

Triacetate **28a**: (79% yield); $[\alpha]_D^{25}$ +7.3 (*c* 1.0 $CHCl_3$); ^1H NMR ($CDCl_3$, 400 MHz), δ (ppm): 7.63 (1H, s, C*H* triazole); 5.43 (1H, d, $J_{3,4}$ 3.0 Hz, H-4); 5.21 (1H, dd, $J_{1,2}$ 8.0 Hz, $J_{2,3}$ 10.5 Hz, H-2); 5.04 (1H, dd, $J_{2,3}$ 10.5 Hz, $J_{3,4}$ 3.0 Hz, H-3); 4.77 (2H, br s, CH_2); 4.60 (1H, dd, $J_{5,6}$ 3.7 Hz, $J_{6,6'}$ 14.2 Hz, H-6); 4.44 (1H, dd, $J_{5,6'}$ 8.4 Hz, $J_{6,6'}$ 14.2 Hz, H-6′); 4.34 (1H, d, $J_{1,2}$ 8.0 Hz, H-1); 4.16 (1H, dd, $J_{5,6}$ 3.7 Hz. $J_{5,6'}$ 8.4 Hz, H-5); 3.42 (3H, s, OCH_3); 2.99 (1H, br s, OH); 2.20, 2.06, 1.99 (9H, 3s, 3 × CH_3). ^{13}C NMR ($CDCl_3$, 100 MHz), δ (ppm): 170.3, 170.1, 169.5 ($COCH_3$); 147.8 (C-quat triazole); 123.1 (*C*H triazole); 102.0 (C-1); 71.8 (C-5); 70.7 (C-3); 68.6 (C-2); 68.0 (C-4); 57.2 (OCH_3); 56.3 (CH_2); 50.2 (C-6); 20.8, 20.7, 20.5 ($COCH_3$). IR (KBr) ν_{max}: 3400,0; 1749.3; 1371.3; 1222.8; 1049.2 cm^{-1}. ESI-MS *m/z*, calcd for $C_{16}H_{23}N_3O_9$ $[M+H]^+$ 402.1; $[M+Na]^+$ 424.1, found 402.1; 424.1. Deprotected compound **28c**: ESI-MS *m/z*, calcd for $C_{10}H_{17}N_3O_6$ $[M+H]^+$ 276.1; $[M+Na]^+$ 298.1, found 276.2; 298.2.

4.4.3. 3-[1-(Methyl 6-deoxy-β-D-galactopyranosid-6-yl)-1*H*-1,2,3-triazol-4-yl]-propan-1-ol (29c)

Triacetate **29a**: (88% yield); ^1H NMR^1H NMR ($CDCl_3$, 400 MHz), δ (ppm): 7.38 (1H, s, CH triazole); 5.40 (1H, d, $J_{3,4}$ 3.2 Hz, H-4); 5.21 (1H, dd, $J_{1,2}$ 7.8 Hz, $J_{2,3}$ 10.5 Hz, H-2); 5.01 (1H, dd, $J_{2,3}$ 10.5 Hz, $J_{3,4}$ 3.2 Hz, H-3); 4.54 (1H, dd, $J_{5,6}$ 4.1 Hz, $J_{6,6'}$ 14.1 Hz, H-6); 4.41 (1H, dd, $J_{5,6'}$ 8.3 Hz, $J_{6,6'}$ 14.1 Hz, H-6′); 4.32 (1H, d, $J_{1,2}$ 7.8 Hz, H-1); 4.13 (1H, dd, $J_{5,6}$ 4.1 Hz, $J_{5,6'}$ 8.3 Hz, H-5); 3.70 (2H, t, *J* 5.9 Hz, CH_2); 3.41 (3H, s, OCH_3); 2.83 (2H, t, *J* 7.3 Hz, CH_2); 2.31 (1H, br s, OH); 2.20, 2.06, 1.98 (9H, 3s, 3 × CH_3); 1.90 (2H, q, *J* 6.7 Hz, CH_2). ^{13}C NMR ($CDCl_3$, 100 MHz), δ (ppm): 170.2; 170.0; 169.5 ($COCH_3$); 147.5 (C-quat triazole); 122.4 (*C*H triazole); 102.1 (C-1); 71.9 (C-5); 70.7 (C-3); 68.6 (C-2); 67.9 (C-4); 61.8 (CH_2OH); 57.2 (OCH_3); 50.0 (C-6); 31.9 (CH_2); 22.0 (CH_2); 20.8, 20.7, 20.5 ($COCH_3$). ESI-MS *m/z*, calcd for $C_{18}H_{27}N_3O_9$ $[M+H]^+$ 430.1; $[M+Na]^+$ 452.1, found 430.2; 452.2. Deprotected compound **29c**: ESI-MS *m/z*, calcd for $C_{12}H_{21}N_3O_6$ $[M+H]^+$ 304.1; $[M+Na]^+$ 326.1, found 304.2; 326.2.

4.4.4. 4-[1-(Methyl 6-deoxy-β-D-galactopyranosid-6-yl)-1*H*-1,2,3-triazol-4-yl]-butan-1-ol (30c)

Triacetate **30a**: (74% yield); ^1H NMR ($CDCl_3$, 400 MHz), δ (ppm): 7.35 (1H, s, C*H* triazole); 5.38 (1H, d, $J_{3,4}$ 3.3 Hz, H-4); 5.21 (1H, dd, $J_{1,2}$ 8.1 Hz, $J_{2,3}$ 10.5 Hz, H-2); 5.00 (1H, dd, $J_{2,3}$ 10.5 Hz, $J_{3,4}$ 3.3 Hz, H-3); 4.54 (1H, dd, $J_{5,6}$ 4.4 Hz, $J_{6,6'}$ 14.2 Hz, H-6); 4.44 (1H, dd, $J_{5,6'}$ 8.2 Hz, $J_{6,6'}$ 14.2 Hz, H-6′); 4.32 (1H, d, $J_{1,2}$ 8.1 Hz, H-1); 4.13 (1H, dd, $J_{5,6}$ 4.4 Hz, $J_{5,6'}$ 8.2 Hz, H-5); 3.65 (2H, t, *J* 6.4 Hz, CH_2); 3.41 (3H, s, OCH_3); 2.75 (2H, t, *J* 7.3 Hz, CH_2); 2.20, 2.04, 1.96 (9H, 3s, 3 × CH_3); 1.89 (1H, br s, OH); 1.75 (2H, q, *J* 7.0 Hz, *J* 7.8 Hz, *J* 7.5 Hz, CH_2); 1.60 (2H, q, *J* 6.3 Hz, *J* 6.6 Hz, *J* 8.2 Hz, CH_2). ^{13}C NMR ($CDCl_3$, 100 MHz), δ (ppm): 170.3, 170.0, 169.5 ($COCH_3$); 148.0 (C-quat triazole); 122.2 (*C*H triazole); 102.1 (C-1); 71.9 (C-5); 70.8 (C-3); 68.5 (C-2); 67.8 (C-4); 62.3 (CH_2OH); 57.1 (OCH_3); 49.8 (C-6); 32.0 (CH_2); 25.5 (CH_2); 25.2 (CH_2); 20.78, 20.7, 20.5 ($COCH_3$). ESI-MS *m/z*, calcd for $C_{19}H_{29}N_3O_9$ $[M+H]^+$ 444.2; $[M+Na]^+$ 466.2, found 444.2; 466.2. Deprotected compound **30c**: ESI-MS *m/z*, calcd for $C_{13}H_{23}N_3O_6$ $[M+H]^+$ 318.1; $[M+Na]^+$ 340.1, found 318.2; 340.2.

4.4.5. [1-(Methyl 6-deoxy-β-D-galactopyranosid-6-yl)-1*H*-1,2,3-triazol-4-yl]-benzene (31c)

Triacetate **31a**: (97% yield); ^1H NMR ($CDCl_3$, 400 MHz), δ (ppm): 7.87 (1H, s, C*H* triazole); 7.82 (2H, d, *J* 7.1 Hz, CH-Ar); 7.43 (2H, pseudo t, *J*∼7.4 Hz, CH-Ar); 7.34 (1H, t, *J* 7.4 Hz, CH-Ar); 5.49 (1H, d, $J_{3,4}$ 3.4 Hz, $J_{4,5}$ 2.8 Hz, H-4); 5.23 (1H, dd, $J_{1,2}$ 8.0 Hz, $J_{2,3}$ 10.4 Hz, H-2); 5.05 (1H, dd, $J_{2,3}$ 10.4 Hz, $J_{3,4}$ 3.4 Hz, H-3); 4.65 (1H, dd, $J_{5,6}$ 3.5 Hz, $J_{6,6'}$ 14.2 Hz, H-6); 4.48 (1H, dd, $J_{5,6'}$ 8.8 Hz, $J_{6,6'}$ 14.2 Hz, H-6′); 4.33 (1H, d, $J_{1,2}$ 8.0 Hz, H-1); 4.18 (1H, dd, $J_{4,5}$ 2.8 Hz, $J_{5,6}$ 3.5 Hz, $J_{5,6'}$ 8.8 Hz, H-5); 3.40 (3H, s, OCH_3); 2.20, 2.09, 2.00 (9H, 3s, 3 × CH_3). ^{13}C NMR ($CDCl_3$, 100 MHz), δ (ppm): 170.3, 170.0, 169.5 ($COCH_3$); 147.8 (C-quat triazole); 130.4 (C-quat Ar); 128.9, 128.2, 125.6, 121.1 (CH-Ar); 102.1 (C-1); 71.9 (C-5); 70.7 (C-3); 68.6 (C-2); 68.0 (C-4); 57.2 (OCH_3); 50.3 (C-6); 20.8, 20.7, 20.5 ($COCH_3$). ESI-MS *m/z*, calcd for $C_{21}H_{25}N_3O_8$ $[M+H]^+$ 448.1; $[M+Na]^+$ 470.1, found 448.1; 470.2. Deprotected compound

31c: ESI-MS *m*/*z*, calcd for $C_{15}H_{19}N_3O_5$ $[M+H]^+$ 322.1; $[M+Na]^+$ 344.1, found 322.2; 344.1.

4.4.6. [1-(Methyl 6-deoxy-β-D-galactopyranosid-6-yl)-1*H*-1,2,3-triazol-4-yl]-phenylmethane (32c)

Triacetate **32a**: (94% yield); ^{1}H NMR ($CDCl_3$, 400 MHz), δ (ppm): 7.28–7.18 (6H, m, CH-Ar, C*H* triazole); 5.41 (1H, d, $J_{3,4}$ 3.3 Hz, H-4); 5.16 (1H, dd, $J_{1,2}$ 8.0 Hz, $J_{2,3}$ 10.3 Hz, H-2); 4.99 (1H, dd, $J_{2,3}$ 10.3 Hz, $J_{3,4}$ 3.3 Hz, H-3); 4.55 (1H, dd, $J_{5,6}$ 3.4 Hz, $J_{6,6'}$ 14.1 Hz, H-6); 4.32 (1H, dd, $J_{5,6'}$ 9.0 Hz, $J_{6,6'}$ 14.1 Hz, H-6′); 4.23 (1H, d, $J_{1,2}$ 8.0 Hz, H-1); 4.11–4.02 (3H, m, H-5, CH_2); 3.21 (3H, s, OCH_3); 2.16, 2.04, 1.97 (9H, 3s, $3 \times CH_3$). ^{13}C NMR ($CDCl_3$, 100 MHz), δ (ppm): 170.1, 170.0, 169.4 (*C*OCH_3); 147.9 (C-quat triazole); 138.9 (C-quat Ar); 128.6, 126.5, 123.0 (CH-Ar); 101.9 (C-1); 71.8 (C-5); 70.7 (C-3); 68.6 (C-2); 67.9 (C-4); 57.0 (O*C*H_3); 50.0 (C-6); 32.2 (*C*H_2); 20.7, 20.6, 20.5 (CO*C*H_3). IR (KBr) ν_{max}: 1751.2; 1454.2; 1244.0; 1047.3 cm^{-1}. ESI-MS *m*/*z*, calcd for $C_{22}H_{27}N_3O_8$ $[M+H]^+$ 462.2; $[M+Na]^+$ 484.1, found 462.1; 484.2. Deprotected compound **32c**: ESI-MS *m*/*z*, calcd for $C_{16}H_{21}N_3O_5$ $[M+H]^+$ 336.1; $[M+Na]^+$ 358.1, found 336.2; 358.2.

4.4.7. [1-(Methyl 6-deoxy-β-D-galactopyranosid-6-yl)-1*H*-1,2,3-triazol-4-yl]-2-phenylmethane (33c)

Triacetate **33a**: (94% yield); ^{1}H NMR ($CDCl_3$, 400 MHz), δ (ppm): 7.29–7.17 (6H, m, CH-Ar, C*H* triazole); 5.40 (1H, d, $J_{3,4}$ 3.4 Hz, H-4); 5.20 (1H, dd, $J_{1,2}$ 8.0 Hz, $J_{2,3}$ 10.3 Hz, H-2); 5.01 (1H, dd, $J_{2,3}$ 10.3 Hz, $J_{3,4}$ 3.4 Hz, H-3); 4.52 (1H, dd, $J_{5,6}$ 3.9 Hz, $J_{6,6'}$ 14.1 Hz, H-6); 4.36 (1H, dd, $J_{5,6'}$ 8.3 Hz, $J_{6,6'}$ 14.1 Hz, H-6′); 4.28 (1H, d, $J_{1,2}$ 8.0 Hz, H-1); 4.09 (1H, dd, $J_{5,6}$ 3.9 Hz, $J_{5,6'}$ 8.3 Hz, H-5); 3.35 (3H, s, OCH_3); 3.07–2.96 (4H, m, CH_2); 2.19, 2.05, 198 (9H, 3s, $3 \times CH_3$). ^{13}C NMR ($CDCl_3$, 100 MHz), δ (ppm): 170.2, 170.0, 169.5 (*C*OCH_3); 147.3 (C-quat triazole); 140.9 (C-quat Ar); 128.4, 126.1, 122.3 (CH-Ar); 102.0 (C-1); 71.9 (C-5); 70.7 (C-3); 68.6 (C-2); 67.9 (C-4); 57.1 (OCH_3); 50.0 (C-6); 35.4 (*C*H_2); 27.2 (*C*H_2); 20.7, 20.6, 20.5 (CO*C*H_3). ESI-MS *m*/*z*, calcd for $C_{23}H_{29}N_3O_8$ $[M+H]^+$ 476.2; $[M+Na]^+$ 498.2, found 476.2; 498.2. Deprotected compound **33c**: ESI-MS *m*/*z*, calcd for $C_{17}H_{23}N_3O_5$ $[M+H]^+$ 350.1; $[M+Na]^+$ 372.1, found 350.2; 372.2.

4.4.8. 2-[1-(Methyl 6-deoxy-β-D-galactopyranosid-6-yl)-1*H*-1,2,3-triazol-4-yl]-aniline (34c)

Triacetate **34a**: (100% yield); ^{1}H NMR ($CDCl_3$, 400 MHz), δ (ppm): 7.85 (1H, s, C*H* triazole); 7.31 (1H, d, $J_{3',4'}$ 7.5 Hz, H-3′); 7.12 (1H, dd, $J_{4',5'}$ 7.2 Hz, $J_{5',6'}$ 8.0 Hz, H-5′); 6.76 (1H, d, $J_{5',6'}$ 8.0 Hz, H-6′); 6.72 (1H, t, *J* 7.5, H-4′); 5.48 (3H, m, H-4, NH_2); 5.22 (1H, dd, $J_{1,2}$ 8.0 Hz, $J_{2,3}$ 10.5 Hz, H-2); 5.04 (1H, dd, $J_{2,3}$ 10.5 Hz, $J_{3,4}$ 3.4 Hz, H-3); 4.63 (1H, dd, $J_{5,6}$ 3.4 Hz, $J_{6,6'}$ 14.1 Hz, H-6); 4.48 (1H, dd, $J_{5,6'}$ 8.8 Hz, $J_{6,6'}$ 14.1 Hz, H-6′); 4.31 (1H, d, $J_{1,2}$ 8.0 Hz, H-1); 4.14 (1H, dd, $J_{5,6}$ 3.4 Hz, $J_{5,6'}$ 8.8 Hz, H-5); 3.39 (3H, s, OCH_3); 2.21, 2.06, 1.99 (9H, 3s, $3 \times CH_3$). ^{13}C NMR ($CDCl_3$, 100 MHz), δ (ppm): 170.3, 170.0, 169.5 (*C*OCH_3); 148.4 (C-quat. triazole); 145.1 (C-2′), 129.1 (C-5′); 127.6 (C-3′); 121.2 (*C*H triazole); 117.4 (C-4′); 116.8 (C-6′); 113.4 (C-1′); 102.1 (C-1); 71.9 (C-5); 70.7 (C-3); 68.6 (C-2); 68.0 (C-4); 57.2 (OCH_3); 50.4 (C-6); 20.8, 20.7, 20.5 (CO*C*H_3). ESI-MS *m*/*z*, calcd for $C_{21}H_{26}N_4O_8$ $[M+H]^+$ 463.2; $[M+Na]^+$ 485.0, found 463.1; 485.1. Deprotected compound **34c**: ESI-MS *m*/*z*, calcd for $C_{15}H_{20}N_4O_5$ $[M+H]^+$ 337.1; $[M+Na]^+$ 359.1, found 337.2; 359.1.

4.4.9. 2-[1-(Methyl 6-deoxy-β-D-galactopyranosid-6-yl)-1*H*-1,2,3-triazol-4-yl]-bromobenzene (35c)

Triacetate **35a**: (100% yield); ^{1}H NMR ($CDCl_3$, 400 MHz), δ (ppm): 8.36 (1H, s, C*H* triazole); 8.14 (1H, d, *J* 7.8 Hz, H-6′); 7.64 (1H, d, *J* 8.0 Hz, H-3′); 7.41 (1H, pseudo t, *J* 7.6 Hz, H-4′); 7.20 (1H, pseudo t, *J* 7.7 Hz, H-5′); 5.52 (1H, d, $J_{3,4}$ 3.3 Hz, H-4); 5.24 (1H, dd, $J_{1,2}$ 7.8 Hz, $J_{2,3}$ 10.3 Hz, H-2); 5.06 (1H, dd, $J_{2,3}$ 10.3 Hz, $J_{3,4}$ 3.3 Hz, H-3); 4.69 (1H, dd, $J_{5,6}$ 3.2 Hz, $J_{6,6'}$ 14.2 Hz, H-6); 4.50 (1H, dd, $J_{5,6'}$ 8.9 Hz, $J_{6,6'}$ 14.2 Hz, H-6′); 4.34 (1H, d, $J_{1,2}$ 7.8 Hz, H-1); 4.21 (1H, dd, $J_{5,6}$ 3.2 Hz, $J_{5,6'}$ 8.9 Hz, H-5); 3.42 (3H, s, OCH_3). 2.23, 2.06, 2.00 (9H, 3s, $3 \times CH_3$). ^{13}C NMR ($CDCl_3$, 100 MHz), δ (ppm): 170.2, 170.0, 169.5 (*C*OCH_3); 145.3 (C-quat triazole); 133.6, 131.0 (C-quat Ar); 130.5, 129.4, 127.7, 124.4 (CH-Ar); 121.0 (*C*H triazole); 102.1 (C-1); 72.0 (C-5); 70.7 (C-3); 68.6 (C-2); 68.0 (C-4); 57.3 (OCH_3); 50.5 (C-6); 20.8, 20.7, 20.5 (CO*C*H_3). ESI-MS *m*/*z*, calcd for $C_{21}H_{24}BrN_3O_8$ $[M+H]^+$ 526.1; $[M+Na]^+$ 548.1, found 526.0; 548.1. Deprotected compound **35c**: ESI-MS *m*/*z*, calcd for $C_{15}H_{18}BrN_3O_5$ $[M+H]^+$ 400.0; $[M+Na]^+$ 422.0, found 400.1; 422.1.

4.4.10. 2-[1-(Methyl 6-deoxy-β-D-galactopyranosid-6-yl)-1*H*-1,2,3-triazol-4-yl]-trifluoromethylbenzene (36c)

Triacetate **36a**: (91% yield); ^{1}H NMR ($CDCl_3$, 400 MHz), δ (ppm): 7.99 (1H, d, *J* 7.8 Hz, H-3′); 7.90 (1H, s, C*H* triazole); 7.75 (1H, d, *J* 7.8 Hz, H-6′); 7.64 (1H, t, *J* 7.8 Hz, H-5′); 7.49 (1H, t, *J* 7.8 Hz, H-4′); 5.68 (1H, d, $J_{3,4}$ 3.5 Hz, H-4); 5.24 (1H, dd, $J_{1,2}$ 8.0 Hz, $J_{2,3}$ 10.5 Hz, H-2); 5.07 (1H, dd, $J_{2,3}$ 10.5 Hz, $J_{3,4}$ 3.5 Hz, H-3); 4.69 (1H, dd, $J_{5,6}$ 2.7 Hz, $J_{6,6'}$ 14.4 Hz, H-6); 4.50 (1H, dd, $J_{5,6'}$ 9.2 Hz, $J_{6,6'}$ 14.4 Hz H-6′); 4.35 (1H, d, $J_{1,2}$ 8.0 Hz, H-1); 4.23 (1H, dd, $J_{5,6}$ 2.7 Hz, $J_{5,6'}$ 9.2 Hz, H-5); 3.44 (3H, s, OCH_3). 2.23, 2.06, 2.00 (9H, 3s, $3 \times CH_3$). ^{13}C NMR ($CDCl_3$, 100 MHz), δ (ppm): 170.2, 170.0, 169.5 (*C*OCH_3); 144.2 (C-quat triazole); 132.1, 131.6 (C-quat Ar); 129.2, 128.3, 127.2, 126.1 (CH-Ar); 123.2 (*C*H triazole); 102.1 (C-1); 72.0 (C-5); 70.7 (C-3); 68.6 (C-2); 68.1 (C-4); 57.1 (O*C*H_3); 50.6 (C-6); 20.8, 20.7, 20.5 (CO*C*H_3). ESI-MS *m*/*z*, calcd for $C_{22}H_{24}F_3N_3O_8$ $[M+H]^+$ 516.1; $[M+Na]^+$ 538.1, found 516.1; 538.1. Deprotected compound **36c**: ESI-MS *m*/*z*, calcd for $C_{16}H_{18}F_3N_3O_5$ $[M+H]^+$ 390.1; $[M+Na]^+$ 412.1, found 390.2; 412.1.

4.4.11. 4-[1-(Methyl 6-deoxy-β-D-galactopyranosid-6-yl)-1*H*-1,2,3-triazol-4-yl]-aniline (37c)

Triacetate **37a**: (92% yield); ^{1}H NMR ($CDCl_3$, 400 MHz), δ (ppm): 7.70 (1H, s, C*H* triazole); 7.59 (2H, d, *J* 8.5 Hz, H-3′, H-5′); 6.72 (2H, d, *J* 8.5 Hz, H-2′, H-6′); 5.47 (1H, d, $J_{3,4}$ 3.3 Hz, H-4); 5.22 (1H, dd, $J_{1,2}$ 8.0 Hz, $J_{2,3}$ 10.5 Hz, H-2); 5.03 (1H, dd, $J_{2,3}$ 10.5 Hz, $J_{3,4}$ 3.3 Hz, H-3); 4.59 (1H, dd, $J_{5,6}$ 3.5 Hz, $J_{6,6'}$ 14.1 Hz, H-6); 4.44 (1H, dd, $J_{5,6'}$ 8.7 Hz, $J_{6,6'}$ 14.1 Hz, H-6′); 4.31 (1H, d, $J_{1,2}$ 8.0 Hz, H-1); 4.13 (1H, dd, $J_{5,6}$ 3.5 Hz, $J_{5,6'}$ 8.7 Hz, H-5); 3.81 (2H, br s, NH_2); 3.39 (3H, s, OCH_3); 2.20, 2.05, 1.99 (9H, 3s, $3 \times CH_3$). ^{13}C NMR ($CDCl_3$, 100 MHz), δ (ppm): 170.3, 170.0, 169.5 (*C*OCH_3); 148.1 (C-4′); 146.7 (C-quat triazole); 126.8 (C-3′, C-5′); 120.7 (C-1′); 119.7 (C-2′, C-6′); 115.2 (*C*H triazole); 102.2 (C-1); 71.9 (C-5); 70.7 (C-3); 68.6 (C-2); 68.0 (C-4); 57.2 (OCH_3); 50.2 (C-6); 20.8–20.5 (CO*C*H_3). ESI-MS *m*/*z*, calcd for $C_{21}H_{26}N_4O_8$ $[M+H]^+$ 463.2; $[M+Na]^+$ 485.0, found 463.2; 485.2. Deprotected compound **37c**: ESI-MS *m*/*z*, calcd for $C_{15}H_{20}N_4O_5$ $[M+H]^+$ 337.1; $[M+Na]^+$ 359.1, found 337.2; 359.1.

4.4.12. 4-[1-(Methyl 6-deoxy-β-D-galactopyranosid-6-yl)-1*H*-1,2,3-triazol-4-yl]-bromobenzene (38c)

Triacetate **38a**: (96% yield); ^{1}H NMR ($CDCl_3$, 400 MHz), δ (ppm): 7.86 (1H, s, C*H* triazole); 7.68 (2H, d, *J* 8.5 Hz, H-2′, H-6′); 7.55 (2H, d, *J* 8.6 Hz, H-3′, H-5′); 5.47 (1H, d, $J_{3,4}$ 3.4 Hz, H-4); 5.23 (1H, dd, $J_{1,2}$ 8.0 Hz, $J_{2,3}$ 10.5 Hz, H-2); 5.05 (1H, dd, $J_{2,3}$ 10.5 Hz, $J_{3,4}$ 3.4 Hz, H-3); 4.65 (1H, dd, $J_{5,6}$ 3.6 Hz, $J_{6,6'}$ 14.4 Hz, H-6); 4.51–4.46 (1H, m, H-6′); 4.33 (1H, d, $J_{1,2}$ 8.0 Hz, H-1); 4.17 (1H, dd, $J_{5,6}$ 3.6 Hz, $J_{5,6'}$ 8.6 Hz, H-5); 3.40 (3H, s, OCH_3). 2.21, 2.06, 2.00 (9H, 3s, $3 \times CH_3$). ^{13}C NMR ($CDCl_3$, 100 MHz), δ (ppm): 170.2, 170.0, 169.5 (*C*OCH_3); 146.8 (C-quat triazole); 132.0, 129.3 (C-quat Ar); 127.1 121.2 (CH Ar); 121.1 (*C*H triazole); 102.1 (C-1); 71.8 (C-5); 70.7 (C-3); 68.5 (C-2); 67.9 (C-4); 57.2 (O*C*H_3); 50.4 (C-6); 20.8, 20.7, 20.5 (CO*C*H_3). ESI-MS *m*/*z*, calcd for $C_{21}H_{24}BrN_3O_8$ $[M+H]^+$ 526.1; $[M+Na]^+$ 548.1, found 526.0; 548.1. Deprotected compound **38c**: ESI-MS *m*/*z*, calcd for $C_{15}H_{18}BrN_3O_5$ $[M+HCOO]^-$ 444.0, found 443.9.

4.4.13. 4-[1-(Methyl 6-deoxy-β-D-galactopyranosid-6-yl)-1*H*-1,2,3-triazol-4-yl]-trifluoromethylbenzene (39c)

Triacetate **39a**: (98% yield); ^{1}H NMR ($CDCl_3$, 400 MHz), δ (ppm): 7.95 (1H, s, C*H* triazole); 7.93 (2H, d, *J* 8.3 Hz, H-3′, H-5′); 7.68 (2H, d, *J* 8.3 Hz, H-2′, H-6′); 5.68 (1H, d, $J_{3,4}$ 3.5 Hz, H-4); 5.23 (1H, dd, $J_{1,2}$ 8.0 Hz, $J_{2,3}$ 10.5 Hz, H-2); 5.05 (1H, dd, $J_{2,3}$ 10.5 Hz, $J_{3,4}$ 3.5 Hz, H-3); 4.68 (1H, dd, $J_{5,6}$ 3.6 Hz, $J_{6,6'}$ 14.2 Hz, H-6); 4.50 (1H, dd, $J_{5,6'}$ 8.7 Hz, $J_{6,6'}$ 14.2 Hz, H-6′); 4.34 (1H, d, $J_{1,2}$ 8.0 Hz, H-1); 4.19 (1H, dd, $J_{5,6}$ 3.6 Hz, $J_{5,6'}$ 8.7 Hz, H-5); 3.40 (3H, s, OCH_3); 2.22, 2.05, 2.00 (9H, 3s, 3 × CH_3). ^{13}C NMR ($CDCl_3$, 100 MHz), δ (ppm): 170.2, 170.0, 169.5 ($COCH_3$); 146.4 (C-quat triazole); 133.8, 130.0 (C-quat Ar); 125.9, 125.7, 124.9, 123.2 (CH Ar); 121.9 (*C*H triazole); 102.2 (C-1); 71.8 (C-5); 70.7 (C-3); 68.6 (C-2); 67.9 (C-4); 57.3 (OCH_3); 50.4 (C-6); 20.8, 20.7, 20.5 ($COCH_3$). ESI-MS *m*/*z*, calcd for $C_{22}H_{24}F_3N_3O_8$ $[M+H]^+$ 516.1; $[M+Na]^+$ 538.1, found 516.1; 538.1. Deprotected compound **39c**: ESI-MS *m*/*z*, calcd for $C_{16}H_{18}F_3N_3O_5$ $[M+H]^+$ 390.1; $[M+Na]^+$ 412.1, found 390.2; 412.1.

4.4.14. 3-[1-(Methyl 6-deoxy-β-D-galactopyranosid-6-yl)-1*H*-1,2,3-triazol-4-yl]-trifluoromethylbenzene (40c)

Triacetate **40a**: (100% yield); ^{1}H NMR ($CDCl_3$, 400 MHz), δ (ppm): 8.08 (1H, s, H-2′); 7.99 (1H, d, *J* 7.6 Hz, H-6′); 7.95 (1H, s, C*H* triazole); 7.60–7.53 (2H, m, H-4′, H-5′); 5.68 (1H, d, $J_{3,4}$ 3.5 Hz, H-4); 5.24 (1H, dd, $J_{1,2}$ 8.0 Hz, $J_{2,3}$ 10.5 Hz, H-2); 5.06 (1H, dd, $J_{2,3}$ 10.5 Hz, $J_{3,4}$ 3.5 Hz, H-3); 4.68 (1H, dd, $J_{5,6}$ 3.5 Hz, $J_{6,6'}$ 14.2 Hz, H-6); 4.50 (1H, dd, $J_{5,6'}$ 8.7 Hz, $J_{6,6'}$ 14.1, Hz H-6′); 4.35 (1H, d, $J_{1,2}$ 8.0 Hz, H-1); 4.21 (1H, dd, $J_{5,6}$ 3.5 Hz, $J_{5,6'}$ 8.7 Hz, H-5); 3.40 (3H, s, OCH_3). 2.22, 2.05, 2.00 (9H, 3s, 3 × CH_3). ^{13}C NMR ($CDCl_3$, 100 MHz), δ (ppm): 170.2, 170.0, 169.5 ($COCH_3$); 146.5 (C-quat triazole); 131.2, 129.4 (C-quat Ar); 128.7, 124.8, 123.0, 122.4 (CH Ar); 121.6 (CH triazole); 102.1 (C-1); 71.8 (C-5); 70.7 (C-3); 68.6 (C-2); 67.9 (C-4); 57.2 (OCH_3); 50.4 (C-6); 20.8, 20.7, 20.5 ($COCH_3$). ESI-MS *m*/*z*, calcd for $C_{22}H_{24}F_3N_3O_8$ $[M+H]^+$ 516.1; $[M+Na]^+$ 538.1, found 516.1; 538.1. Deprotected compound **40c**: ESI-MS *m*/*z*, calcd for $C_{16}H_{18}F_3N_3O_5$ $[M+H]^+$ 390.1; $[M+Na]^+$ 412.1, found 390.2; 412.1.

4.4.15. [1-(Methyl 6-deoxy-β-D-galactopyranosid-6-yl)-1*H*-1,2,3-triazol-4-yl]-*N*-phthalimidylmethane (41c)

Triacetate **41a**: (100% yield); ^{1}H NMR ($CDCl_3$, 400 MHz), δ (ppm): 7.87–7.70 (4H, m, CH Ar); 7.69 (1H, s, C*H* triazole); 5.44 (1H, d, $J_{3,4}$ 3.3 Hz, H-4); 5.18 (1H, dd, $J_{1,2}$ 8.0 Hz, $J_{2,3}$ 10.2 Hz, H-2); 5.01 (1H, d, *J* 15.3 Hz, CH_2); 5.00 (1H, dd, $J_{2,3}$ 10.2 Hz, $J_{3,4}$ 3.4 Hz, H-3); 4.97 (1H, d, *J* 15.3 Hz, CH_2); 4.60 (1H, dd, $J_{5,6}$ 3.0 Hz, $J_{6,6'}$ 14.2 Hz, H-6); 4.37 (1H, dd, $J_{5,6'}$ 9.0 Hz, $J_{6,6'}$ 14.2 Hz, H-6′); 4.26 (1H, d, $J_{1,2}$ 8.0 Hz, H-1); 4.07 (1H, dd, $J_{5,6}$ 3.0 Hz, $J_{5,6'}$ 9.0 Hz, H-5); 3.30 (3H, s, OCH_3). δ (ppm): 170.2, 169.9, 169.5 ($COCH_3$); 167.5; 166.9 (*C*O); 142.9 (C-quat triazole); 134.2, 132.0, 124.3 (CH Ar); 129.9, 128.2 (C-quat Ar); 123.4 (*C*H triazole); 101.9 (C-1); 71.8 (C-5); 70.6 (C-3); 68.6 (C-2); 67.9 (C-4); 57.1 (OCH_3); 50.3 (C-6); 33.0 (CH_2); 20.8, 20.6, 20.5 ($COCH_3$). ESI-MS *m*/*z*, calcd for $C_{24}H_{26}N_4O_{10}$ $[M+H]^+$ 531.1; $[M+Na]^+$ 553.1, found 531.2; 553.2. Deprotected compound **41c**: ESI-MS *m*/*z*, calcd for $C_{18}H_{20}N_4O_7$ $[M+Na]^+$ 427.1, found 427.2.

4.4.16. 2-[1-(Methyl 6-deoxy-β-D-galactopyranosid-6-yl)-1*H*-1,2,3-triazol-4-yl]-pyridine (42c)

Triacetate **42a**: (100% yield); ^{1}H NMR ($CDCl_3$, 400 MHz), δ (ppm): 8.58 (1H, d, $J_{4',5'}$ 4.1 Hz, H-6′); 8.23 (1H, C*H* triazole) 8.15 (1H, d, $J_{2',3'}$ 8.0 Hz, H-3′); 7.77 (1H, dt, $J_{2',3'}$ 8.0 Hz, $J_{3',4'}$ 1.7 Hz, H-4′); 7.23 (1H, m, H-5′); 5.47 (1H, d, $J_{4,5}$ 2.8 Hz, H-4); 5.23 (1H, dd, $J_{1,2}$ 8.0 Hz, $J_{2,3}$ 10.5 Hz, H-2); 5.05 (1H, dd, $J_{2,3}$ 10.5 Hz, $J_{3,4}$ 3.4 Hz, H-3); 4.66 (1H, dd, $J_{5,6}$ 3.6 Hz, $J_{6,6'}$ 14.1 Hz, H-6); 4.51 (1H, dd, $J_{5,6'}$ 8.5 Hz, $J_{6,6'}$ 14.1 Hz, H-6′); 4.34 (1H, d, $J_{1,2}$ 8.0 Hz, H-1); 4.20 (1H, dd, $J_{4,5}$ 2.8 Hz, $J_{5,6'}$ 8.5, H-5); 3.54 (3H, s, OCH_3); 2.22, 2.06, 1.99 (9H, 3s, 3 × CH_3). ^{13}C NMR ($CDCl_3$, 100 MHz), δ (ppm): 170.2, 170.0, 169.5 ($COCH_3$); 150.0 (C-2′), 149.52 (C-6′) 148.5 (C-quat triazole); 136.0 (C-4′), 127.4 (C-3′), 123,3 (C-5′); 120.2 (*C*H triazole); 102.0 (C-1); 71.8 (C-5); 70.7 (C-3); 68.6 (C-2); 67.9 (C-4); 57.0 (OCH_3); 50.4 (C-6); 20.8, 20.7, 20.5 ($COCH_3$). ESI-MS *m*/*z*, calcd for $C_{20}H_{24}N_4O_8$ $[M+H]^+$ 449.1; $[M+Na]^+$ 471.1, found 449.1; 471.2. Deprotected compound **42c**: ESI-MS *m*/*z*, calcd for $C_{14}H_{18}N_4O_5$ $[M+H]^+$ 323.1; $[M+Na]^+$ 346.1, found 323.2; 345.2.

4.4.17. 3-[1-(Methyl 6-deoxy-β-D-galactopyranosid-6-yl)-1*H*-1,2,3-triazol-4-yl]-pyridine (43c)

Triacetate **43a**: (85% yield); ^{1}H NMR ($CDCl_3$, 400 MHz), δ (ppm): 8.98 (1H, s, C*H*Py, H-2′); 8.58 (1H, d, $J_{5',6'}$ 4.8 Hz, H-6′); 8.20 (1H, dd, $J_{4',5'}$ 8.0 Hz, $J_{4',6'}$ 1.7 Hz H-4′); 7.96 (1H, C*H* triazole); 7.38 (1H, dd, $J_{4',5'}$ 8.0 Hz, $J_{5',6'}$ 4.8 Hz, H-5′); 5.49 (1H, d, $J_{3,4}$ 3.4 Hz, H-4); 5.24 (1H, dd, $J_{1,2}$ 8.0 Hz, $J_{2,3}$ 10.3 Hz, H-2); 5.05 (1H, dd, $J_{2,3}$ 10.3 Hz, $J_{3,4}$ 3.4 Hz, H-3); 4.68 (1H, dd, $J_{5,6}$ 3.6 Hz, $J_{6,6'}$ 14.1 Hz, H-6); 4.51 (1H, dd, $J_{5,6'}$ 8.5 Hz, $J_{6,6'}$ 14.1 Hz, H-6′); 4.34 (1H, d, $J_{1,2}$ 8.0 Hz, H-1); 4.19 (1H, dd, $J_{5,6}$ 3.6 Hz, $J_{5,6'}$ 8.5, H-5); 3.40 (3H, s, OCH_3); 2.22, 2.02, 2.04 (9H, 3s, 3 × CH_3). ^{13}C NMR ($CDCl_3$, 100 MHz), δ (ppm): 170.2, 170.0, 169.5 ($COCH_3$); 149.4 (C-6′) 146.9 (C-2′); 144.7 (C-quat triazole); 132.9 (C-4′); 126.5 (C-3′), 123.8 (C-5′), 121.4 (*C*H triazole); 102.1 (C-1); 71.8 (C-5); 70.6 (C-3); 68.5 (C-2); 67.9 (C-4); 57.2 (OCH_3); 50.4 (C-6); 20.8, 20.7, 20.5 ($COCH_3$). IR (KBr) ν_{max}: 1749.3; 1369.4; 1220.9; 1047.3 cm^{-1}. ESI-MS *m*/*z*, calcd for $C_{20}H_{24}N_4O_8$ $[M+H]^+$ 449.1; $[M+Na]^+$ 471.1, found 449.2; 471.1. Deprotected compound **43c**: ESI-MS *m*/*z*, calcd for $C_{14}H_{18}N_4O_5$ $[M+H]^+$ 323.1; $[M+Na]^+$ 346.1, found 323.2; 345.1.

4.4.18. *N*-Benzyl-*N*-methyl-1-[1-(methyl 6-deoxy-β-D-galactopyranosid-6-yl)-1*H*-1,2,3-triazol-4-yl]-methylamine (44c)

Triacetate **44a**: (70% yield); ^{1}H NMR ($CDCl_3$, 400 MHz), δ (ppm): 7,56 (1H, s, C*H* triazole); 7.31–7.22 (5H, m, CH Ar); 5.44 (1H, d, $J_{3,4}$ 3.2 Hz, H-4); 5.21 (1H, dd, $J_{1,2}$ 8.0 Hz, $J_{2,3}$ 10.5 Hz, H-2); 5.02 (1H, dd, $J_{2,3}$ 10.5 Hz, $J_{3,4}$ 3.2 Hz, H-3); 4.58 (1H, dd, $J_{5,6}$ 3.7 Hz, $J_{6,6'}$ 14.1 Hz, H-6); 4.42 (1H, dd, $J_{5,6'}$ 8.8 Hz, $J_{6,6'}$ 14.1 Hz, H-6′); 4.29 (1H, d, $J_{1,2}$ 8.0 Hz, H-1); 4.15 (1H, dd, $J_{5,6}$ 3.7 Hz, $J_{5,6'}$ 8.8 Hz, H-5); 3.71 (2H, s, CH_2); 3.54 (2H, s, CH_2); 3.31 (3H, s, OCH_3). 2.21, 2.20, 2.05, 1.99 (12H, 4s, 4 × CH_3). ^{13}C NMR ($CDCl_3$, 100 MHz), δ (ppm): 170.2, 170.0, 169.5 ($COCH_3$); 145.5 (C-quat triazole); 138.7 (C-quat Ar); 128.8, 128.2, 127.0 (CH Ar); 123.9 (*C*H triazole); 102.1 (C-1); 71.9 (C-5); 70.7 (C-3); 68.6 (C-2); 67.9 (C-4); 61.4 (CH_2); 57.1 (O*C*H$_3$); 52.0 (*C*H$_2$); 50.2 (C-6); 42.1 (N*C*H$_3$); 20.8, 20.6, 20.5 ($COCH_3$). ESI-MS *m*/*z*, calcd for $C_{24}H_{32}N_4O_8$ $[M+H]^+$ 505.2; $[M+Na]^+$ 527.2, found 505.2; 527.2. Deprotected compound **44c**: ESI-MS *m*/*z*, calcd for $C_{18}H_{26}N_4O_5$ $[M+H]^+$ 379.2; $[M+Na]^+$ 401.2, found 379.2; 401.2.

4.4.19. 4-[1-(Methyl 6-deoxy-β-D-galactopyranosid-6-yl)-1*H*-1,2,3-triazol-4-yl]-butanoic acid (45c)

Triacetate **45a**: (82% yield); ^{1}H NMR ($CDCl_3$, 400 MHz), δ (ppm): 7.41 (1H, s, C*H* triazole); 5.41 (1H, d, $J_{3,4}$ 3.2 Hz, H-4); 5.21 (1H, dd, $J_{1,2}$ 8.0 Hz, $J_{2,3}$ 10.3 Hz, H-2); 5.02 (1H, dd, $J_{2,3}$ 10.3 Hz, $J_{3,4}$ 3.2 Hz, H-3); 4.57 (1H, dd, $J_{5,6}$ 3.9 Hz, $J_{6,6'}$ 14.2 Hz, H-6); 4.41 (1H, dd, $J_{5,6'}$ 8.7 Hz, $J_{6,6'}$ 14.2 Hz, H-6′); 4.32 (1H, d, $J_{1,2}$ 8.0 Hz, H-1); 4.13 (1H, dd, $J_{5,6}$ 3.9 Hz, $J_{5,6'}$ 8.7 Hz, H-5); 3.41 (3H, s, OCH_3); 2.80 (2H, t, *J* 7.3 Hz, CH_2); 2.41 (2H, t, *J* 7.3 Hz, CH_2); 2.21, 2.06, 1.99 (9H, 3s, 3 × CH_3); 2.06–1.99 (2H, m, CH_2). ^{13}C NMR ($CDCl_3$, 100 MHz), δ (ppm): 177.8 (CO_2H); 170.3, 170.0, 169.5 ($COCH_3$); 147.0 (C-quat triazole); 122.6 (*C*H triazole); 102.0 (C-1); 71.9 (C-5); 70.7 (C-3); 68.6 (C-2); 67.9 (C-4); 57.2 (O*C*H$_3$); 50.1 (C-6); 33.1 (*C*H$_2$); 24.5 (*C*H$_2$); 24.3 (*C*H$_2$); 20.8, 20.7, 20.5 ($COCH_3$). IR (KBr) ν_{max}: 2939.3; 1747.4; 1222.8; 1064.6 cm^{-1}. ESI-MS *m*/*z*, calcd for $C_{19}H_{27}N_3O_{10}$ $[M+H]^+$ 458.2, found 458.2. Deprotected compound **45c**: ESI-MS *m*/*z*, calcd for $C_{13}H_{21}N_3O_7$ $[M+H]^+$ 332.1; $[M+Na]^+$ 354.1, found 332.1, 354.2.

4.4.20. (2*R*/*S*)-1-[1-(Methyl 6-deoxy-β-D-galactopyranosid-6-yl)-1*H*-1,2,3-triazol-4-yl]-propan-2-ol (46c)

Triacetate **46a**: (85% yield); ^{1}H NMR ($CDCl_3$, 400 MHz), δ (ppm): 7.45 (1H, s, C*H* triazole); 5.39 (1H, dd, $J_{3,4}$ 3.4 Hz, $J_{4,5}$ 8.3 Hz, H-4); 5.21 (1H, dd, $J_{1,2}$ 7.8 Hz, $J_{2,3}$ 10.5 Hz, H-2); 5.02 (1H, dd, $J_{2,3}$ 10.5 Hz, $J_{3,4}$ 3.4 Hz, H-3); 4.56 (1H, dt, $J_{5,6}$ 4.2 Hz, $J_{6,6'}$ 14.1 Hz, H-6); 4.44 (1H, dd, $J_{5,6'}$ 9.5 Hz, $J_{6,6'}$ 14.1 Hz, H-6′); 4.33 (1H, d, $J_{1,2}$ 7.8 Hz, H-1); 4.18–4.14 (2H, m, H-5, C*H*OH); 3.43 (3H, s, OCH_3); 2.87 (1H, dd, *J* 3.5 Hz, *J* 15.0 Hz, CH_2); 2.75 (1H, dd, *J* 8.3 Hz, *J* 15.0 Hz, CH_2); 2.20, 2.04, 1.98 (9H, 3s, 3 × $COCH_3$); 1.27–1.24 (3H, m, CH(OH)C*H*$_3$). ^{13}C NMR ($CDCl_3$, 100 MHz), δ (ppm): 170.3, 170.0, 169.5 (*C*OCH_3); 145.2 (C-quat triazole); 123.3 (*C*H triazole); 102.1 (C-1); 71.8 (C-5); 70.7 (C-3); 68.6 (C-2); 67.8 (C-4); 67.1, 67.0 (*C*HOH); 57.2 (OCH_3); 50.0 (C-6); 34.8, 34.7 (*C*H_2CHOH); 22.9 (CH(OH)*C*H_3); 20.8, 20.7, 20.5 (CO*C*H_3). ESI-MS *m*/*z*, calcd for $C_{18}H_{27}N_3O_9$ $[M+H]^+$ 430.1; $[M+Na]^+$ 452.1, found 430.2; 452.2. Deprotected compound **46c**: ESI-MS *m*/*z*, calcd for $C_{12}H_{21}N_3O_6$ $[M+H]^+$ 304.1; $[M+Na]^+$ 326.1, found 304.2; 326.2.

4.4.21. (1*R*/*S*)-1-[1-(Methyl 6-deoxy-β-D-galactopyranosid-6-yl)-1*H*-1,2,3-triazol-4-yl]-propan-1-ol (47c)

Triacetate **47a**: (89% yield); ^{1}H NMR ($CDCl_3$, 400 MHz), δ (ppm): 7.55 (1H, s, C*H* triazole); 5.43 (1H, br s, H-4); 5.21 (1H, dd, $J_{1,2}$ 7.8 Hz, $J_{2,3}$ 10.5 Hz, H-2); 5.03 (1H, dd, $J_{2,3}$ 10.5 Hz, $J_{3,4}$ 3.2 Hz, H-3); 4.80 (1H, m, C*H*OH); 4.59 (1H, d_{app} $J_{6,6'}$ 14.1 Hz, H-6); 4.41 (1H, dd, $J_{5,6'}$ 8.6 Hz, $J_{6,6'}$ 14.1 Hz, H-6′); 4.33, 4.32 (1H, 2 × d, $J_{1,2}$ 7.8 Hz, H-1); 4.15 (1H, m, H-5); 3.40, 3.39 (3H, s, OC*H*$_3$); 2.73 (1H, br s, OH); 2.20, 2.06, 1.98 (9H, 3s, 3 × CH_3); 1.88 (2H, q, *J* 6.4 Hz, *J* 7.2 Hz, C*H*$_2$); 0.96 (3H, t, *J* 7.2 Hz, CH_3). ^{13}C NMR ($CDCl_3$, 100 MHz), δ (ppm): 170.3; 170.0; 169.5 (*C*OCH_3); 151.3 (C-quat triazole); 122.0, 121.9 (*C*H triazole); 102.0 (C-1); 71.9 (C-5); 70.7 (C-3); 68.6 (C-2); 68.2 (*C*HOH); 67.9 (C-4); 57.1 (O*C*H$_3$); 50.2, 50.1 (C-6); 30.3, 30.2 (*C*H_2CH$_3$); 20.8, 20.7, 20.5 (CO*C*H_3); 9.7 (CH$_2$*C*H$_3$). ESI-MS *m*/*z*, calcd for $C_{18}H_{27}N_3O_9$ $[M+H]^+$ 430.1; $[M+Na]^+$ 452.1, found 430.1; 452.2. Deprotected compound **47c**: ESI-MS *m*/*z*, calcd for $C_{12}H_{21}N_3O_6$ $[M+H]^+$ 304.1; $[M+Na]^+$ 326.1, found 304.2; 326.1.

4.4.22. 1,3-Bis{1-[(methyl 6-deoxy-β-D-galactopyranosid-6-yl)]-1*H*-1,2,3-triazol-6-yl}-propane (48c)

Triacetate **48a**: (33% yield); ^{1}H NMR ($CDCl_3$, 400 MHz), δ (ppm): 7.39 (2H, s, C*H* triazole); 5.40 (2H, d, $J_{3,4}$ 3.4 Hz, H-4); 5.21 (2H, dd, $J_{1,2}$ 8.0 Hz, $J_{2,3}$ 10.5 Hz, H-2); 5.02 (2H, $J_{2,3}$ 10.5 Hz, $J_{3,4}$ 3.4 Hz, H-3); 4.55 (2H, m, H-6); 4.40 (2H, dd, $J_{5,6'}$ 8.3 Hz, $J_{6,6'}$ 14.1 Hz, H-6′); 4.32 (2H, d, $J_{1,2}$ 8.0 Hz, H-1); 4.13 (2H, m, H-5); 3.41 (6H, s, OC*H*$_3$); 2.75 (4H, t, *J* 7.3 Hz, C*H*$_2$); 2.20, 2.06, 1.98 (18H, 3s, 3 × CH_3); 2.13–1.98 (2H, m, C*H*$_2$). ^{13}C NMR ($CDCl_3$, 100 MHz), δ (ppm): 170.1, 169.8, 169.4 (*C*OCH_3); 147.3 (C-quat triazole); 122.4 (*C*H triazole); 102.0 (C-1); 71.8 (C-5); 70.7 (C-3); 68.7 (C-2); 67.7 (C-4); 57.0 (O*C*H$_3$); 49.9 (C-6); 29.6 (*C*H_2); 24.4 (2 × *C*H_2); 20.7, 20.5, 20.3 (CO*C*H_3). ESI-MS *m*/*z*, calcd for $C_{33}H_{46}N_6O_{16}$ $[M+H]^+$ 783.3; $[M+Na]^+$ 805.3, found 783.4; 805.3. Deprotected compound **48c**: ESI-MS *m*/*z*, calcd for $C_{21}H_{34}N_6O_{10}$ $[M+Na]^+$ 553.2, found 553.3.

4.4.23. Methyl [1-(methyl 6-deoxy-β-D-galactopyranosid-6-yl)-1*H*-1,2,3-triazol-4-yl]-carboxylate (49c)

Triacetate **49a**: (96% yield); ^{1}H NMR ($CDCl_3$, 400 MHz), δ (ppm): 8.20 (1H, s, C*H* triazole); 5.49 (1H, d, $J_{3,4}$ 3. Hz, H-4); 5.22 (1H, dd, $J_{1,2}$ 7.8 Hz, $J_{2,3}$ 10.5 Hz, H-2); 5.04 (1H, dd, $J_{2,3}$ 10.5 Hz, $J_{3,4}$ 3.3 Hz, H-3); 4.69 (1H, dd, $J_{5,6}$ 3.4 Hz, $J_{6,6'}$ 14.2 Hz, H-6); 4.49 (1H, dd, $J_{5,6'}$ 8.7 Hz, $J_{6,6'}$ 14.2 Hz, H-6′); 4.32 (1H, d, $J_{1,2}$ 7.8 Hz, H-1); 4.17 (1H, dd, $J_{5,6}$ 3.4, $J_{5,6'}$ 8.7 Hz, H-5); 3.95 (3H, s, CO_2CH3); 3.39 (3H, s, OC*H*$_3$); 2.20, 2.04, 1.97 (9H, 3s, 3 × CH_3). ^{13}C NMR ($CDCl_3$, 100 MHz), δ (ppm): 170.3; 170.0; 169.5 (*C*OCH_3); 161.0 (*C*O$_2$CH$_3$); 140.0 (C-quat triazole); 128.9 (*C*H triazole); 102.1 (C-1); 71.5 (C-5); 70.6 (C-3); 68.5 (C-2); 67.9 (C-4); 57.2 (O*C*H$_3$); 52.3 (CO$_2$*C*H$_3$); 50.7 (C-6); 20.7, 20.6, 20.5 (CO*C*H_3). IR (KBr) ν_{max}: 1749.3; 1371.3; 1222.8; 1070.4 cm^{-1}. ESI-MS *m*/*z*, calcd for $C_{17}H_{23}N_3O_{10}$ $[M+H]^+$ 430.1; $[M+Na]^+$ 452.1, found 430.0; 452.1. Deprotected compound **49c**: ESI-MS *m*/*z*, calcd for $C_{11}H_{17}N_3O_7$ $[M+H]^+$ 304.1; $[M+Na]^+$ 326.1, found 304.1; 326.1.

4.4.24. [1-(Methyl 6-deoxy-β-D-galactopyranosid-6-yl)-1*H*-1,2,3-triazol-4-yl]-methanol *O*-(*R*/*S*)-epoxypropyl ether (50c)

Triacetate **50a**: (86% yield); ^{1}H NMR ($CDCl_3$, 400 MHz), δ (ppm): 7.65 (1H, s, CH triazole); 5.42 (1H, br s, H-4); 5.24–5.20 (1H, ddd, $J_{1,2}$ 8.0, $J_{2,3}$ 10.2 Hz, *J* 2.4 Hz, H-2); 5.02 (1H, dd, $J_{2,3}$ 10.2 Hz, $J_{3,4}$ 3.0 Hz, H-3); 4.71–4.69 (2H, m, C*H*$_2$); 4.59 (1H, dd, $J_{5,6}$ 3.7 Hz, $J_{6,6'}$ 14.2 Hz, H-6); 4.44 (1H, dd, $J_{5,6'}$ 8.4 Hz, $J_{6,6'}$ 14.2 Hz, H-6′); 4.32 (1H, d, $J_{1,2}$ 8.0 Hz, H-1); 4.13 (1H, dd, $J_{5,6}$ 3.7 Hz, $J_{5,6'}$ 8.4 Hz, H-5); 3.84 (1H, dt, *J* 2.0 Hz, *J* 2.44, *J* 11.4 Hz, C*H*$_2$); 3.45–3.14 (1H, m, C*H*$_2$); 3.40 (1H, s, OC*H*$_3$); 3.16–3.15 (1H, m, C*H*); 2.80–2.78 (1H, m, C*H*$_2$); 2.62–2.60 (1H, m, C*H*$_2$). ^{13}C NMR ($CDCl_3$, 100 MHz), δ (ppm): 170.3; 170.0; 169.5 (*C*OCH_3); 144.9 (C-quat triazole); 124.1 (*C*H triazole); 102.0 (C-1); 71.8 (C-5); 71.0 (*C*H_2); 70.7 (C-3); 68.6 (C-2); 67.9 (C-4); 64.5 (*C*H_2); 57.2 (O*C*H$_3$); 50.6 (*C*H); 50.2 (C-6); 44.1 (*C*H_2); 20.8, 20.6, 20.5 (CO*C*H_3). IR (KBr) ν_{max}: 1749.3; 1369.4; 1222.8; 1047.3 cm^{-1}. ESI-MS *m*/*z*, calcd for $C_{19}H_{27}N_3O_{10}$ $[M+H]^+$ 458.1, found 458.2. Deprotected compound **50c**: ESI-MS *m*/*z*, calcd for $C_{13}H_{21}N_3O_7$ $[M+H]^+$ 332.1, found 332.2.

4.4.25. [1-(β-D-Galactopyranosyl)-1*H*-1,2,3-triazol-4-yl]-methanol (28d)

Tetraacetate **28b**: (91% yield); $[\alpha]_D^{25}$ +4.0 (*c* 1.0 $CHCl_3$); ^{1}H NMR ($CDCl_3$, 400 MHz), δ (ppm): 7.86 (1H, s, C*H* triazole); 5.86 (1H, d, $J_{1,2}$ 9.3 Hz, H-1); 5.55 (1H, pseudo t, *J* 9.7 Hz, H-2); 5.56 (1H, d, $J_{3,4}$ 3.2 Hz, H-4); 5.26 (1H, dd, $J_{2,3}$ 10.5 Hz, $J_{3,4}$ 3.2 Hz, H-3); 4.81 (2H, d, *J* 5.6 Hz, CH_2); 4.24 (1H, pseudo t, J 6.3 Hz, H-5); 4.21 (1H, dd, $J_{5,6}$ 5.6 Hz, $J_{6,6'}$ 11.4 Hz, H-6); 4.14 (1H, dd, $J_{5,6'}$ 7.1 Hz, $J_{6,6'}$ 11.4 Hz, H-6′); 2.72 (1H, t, *J* 5.6 Hz, OH); 2.22, 2.04, 2.01, 1.89 (14H, 4s, 4 × CH_3). ^{13}C NMR ($CDCl_3$, 100 MHz), δ (ppm): 170.4, 170.0, 169.8, 169.2 (*C*OCH_3); 148.4 (C-quat triazole); 120.2 (*C*H triazole); 86.2 (C-1); 74.0 (C-5); 70.8 (C-3); 67.9 (C-2); 66.9 (C-4); 61.2 (C-6); 56.5 (CH_2); 20.7, 20.5, 20.3 (CO*C*H_3). IR (KBr) ν_{max}: 3400,0, 1753.2; 1371.3; 1222.8; 1060.8 cm^{-1}. ESI-MS *m*/*z*, calcd for $C_{17}H_{23}N_3O_{10}$ $[M+H]^+$ 430.1; $[M+Na]^+$ 452.1, found 430.0; 452.1. Deprotected compound **28d**: ESI-MS *m*/*z*, calcd for $C_9H_{15}N_3O_6$ $[M+Na]^+$ 284.1, found 284.1.

4.4.26. 3-[1-(β-D-Galactopyranosyl)-1*H*-1,2,3-triazol-4-yl]-propan-1-ol (29d)

Tetraacetate **29b**: (100% yield); ^{1}H NMR ($CDCl_3$, 400 MHz), δ (ppm): 7.64 (1H, s, C*H* triazole); 5.83 (1H, d, $J_{1,2}$ 9.5 Hz, H-1); 5.55 (1H, d, $J_{3,4}$ 3.4 Hz, H-4); 5.51 (1H, pseudo t, *J* 9.8 Hz, H-2); 5.26 (1H, dd, $J_{2,3}$ 10.2 Hz, $J_{3,4}$ 3.4 Hz, H-3); 4.24 (1H, t, *J* 6.4 Hz, H-5); 4.20 (1H, dd, $J_{5,6}$ 5.9 Hz, $J_{6,6'}$ 11.4 Hz, H-6); 4.15 (1H, dd, $J_{5,6'}$ 6.9 Hz, $J_{6,6'}$ 11.4 Hz, H-6′); 3.69 (2H, t, *J* 6.3 Hz, CH_2); 2.87 (2H, t, *J* 7.3 Hz, CH_2); 2.35 (1H, br s, OH); 2.22, 2.06, 2.05, 1.89 (12H, 4s, 4 × CH_3); 1.95 (2H, q, *J* 6.3 Hz, *J* 7.3 Hz, CH_2). ^{13}C NMR ($CDCl_3$, 100 MHz), δ (ppm): 170.4, 170.0, 169.8, 169.2 (*C*OCH_3); 148.2 (C-quat triazole); 119.4 (*C*H triazole); 86.2 (C-1); 74.0 (C-5); 70.7 (C-3); 67.9 (C-2); 66.9 (C-4); 61.5 (*C*H_2OH); 61.2 (C-6); 31.7 (CH_2); 22.0 (CH_2); 20.7, 20.5, 20.2 (CO*C*H_3). ESI-MS *m*/*z*, calcd for $C_{19}H_{27}N_3O_{10}$ $[M+H]^+$ 458.1; $[M+Na]^+$ 480.1, found 458.0; 480.1. Deprotected compound **29d**: ESI-MS *m*/*z*, calcd for $C_{11}H_{19}N_3O_6$ $[M+Na]^+$ 312.1, found 312.2.

4.4.27. 4-[1-(β-D-Galactopyranosyl)-1*H*-1,2,3-triazol-4-yl]-butan-1-ol (30d)

Tetraacetate **30b**: (86% yield); ^{1}H NMR ($CDCl_3$, 400 MHz), δ (ppm): 7.61 (1H, s, C*H* triazole); 5.82 (1H, d, $J_{1,2}$ 9.3 Hz, H-1); 5.55 (1H, m, H-4); 5.53 (1H, pseudo t, *J* 9.7 Hz, H-2); 5.25 (1H, dd, $J_{2,3}$ 10.2 Hz, $J_{3,4}$ 3.4 Hz, H-3); 4.23 (1H, t, *J* 6.4 Hz, H-5); 4.19

(1H, dd, $J_{5,6}$ 5.9 Hz, $J_{6,6'}$ 11.4 Hz, H-6); 4.15 (1H, dd, $J_{5,6'}$ 6.9 Hz, $J_{6,6'}$ 11.4 Hz, H-6′); 3.66 (2H, t, *J* 6.3 Hz, CH_2OH); 2.77 (2H, t, *J* 7.3 Hz, CH_2); 2.26, 2.05, 2.01, 1.88 (12H, 4s, 4 × CH_3); 1.92 (1H, br s, OH); 1.80 (2H, q, *J* 6.8 Hz, *J* 7.3 Hz, *J* 7.5 Hz, CH_2); 1.57 (2H, q, *J* 6.8 Hz, *J* 6.6 Hz, *J* 7.0 Hz, CH_2). ^{13}C NMR ($CDCl_3$, 100 MHz), δ (ppm): 170.4, 170.0, 169.8, 169.3 (*C*OCH_3); 148.7 (C-quat triazole); 119.1 (*C*H triazole); 86.2 (C-1); 73.9 (C-5); 70.8 (C-3); 67.9 (C-2); 66.9 (C-4); 62.2 (*C*H_2OH); 61.2 (C-6); 31.9 (*C*H_2); 25.3 (*C*H_2); 25.2 (*C*H_2); 20.7, 20.6, 20.5, 20.2 (CO*C*H_3). ESI-MS *m*/*z*, calcd for $C_{20}H_{29}N_3O_{10}$ $[M+H]^+$ 472.1; $[M+Na]^+$ 494.1, found 472.0; 494.2. Deprotected compound **30d**: ESI-MS *m*/*z*, calcd for $C_{12}H_{21}N_3O_6$ $[M+Na]^+$ 326.1, found 326.2.

4.4.28. [1-(β-D-Galactopyranosyl)-1*H*-1,2,3-triazol-4-yl]-benzene (31d)

Tetraacetate **31b**: (93% yield); ^{1}H NMR ($CDCl_3$, 400 MHz), δ (ppm): 8,05 (1H, s, C*H* triazole); 7.90 (2H, d, *J* 7.1 Hz, CH Ar); 7.45 (2H, pseudo t, *J* 7,3 Hz, CH Ar); 7.36 (1H, t, *J* 7.3 Hz, CH Ar); 5.90 (1H, d, $J_{1,2}$ 9.5 Hz, H-1); 5,64 (1H, pseudo t, *J* 10.0 Hz, H-2); 5.58 (1H, d, *J* 2.7 Hz, H-4); 5.29 (1H, dd, $J_{2,3}$ 10.5 Hz, $J_{3,4}$ 3.3 Hz, H-3); 4.18 (3H, m, H-6, H-6′, H-5); 2.25, 2.06, 2.05, 1.90 (12H, 4s, 4 × CH_3). ^{13}C NMR ($CDCl_3$, 100 MHz), δ (ppm): 170.4, 170.0, 169.8, 169.2 (*C*OCH_3); 148.5 (C-quat); 129.9, 128.8, 128.5, 125.9 (CH Ar); 117.8 (*C*H triazole); 86.3 (C-1); 74.1 (C-5); 70.9 (C-3); 67.7 (C-2); 66.9 (C-4); 61.2 (C-6); 20.7, 20.6, 20.5, 20.3 (CO*C*H_3). ESI-MS *m*/*z*, calcd for $C_{22}H_{25}N_3O_9$ $[M+H]^+$ 476.1; $[M+Na]^+$ 498.1, found 476.0; 498.1. Deprotected compound **31d**: ESI-MS *m*/*z*, calcd for $C_{14}H_{17}N_3O_5$ $[M+Na]^+$ 330.1, found 330.1.

4.4.29. [1-(β-D-Galactopyranosyl)-1*H*-1,2,3-triazol-4-yl]-phenylmethane (32d)

Tetraacetate **32b**: (81% yield); ^{1}H NMR ($CDCl_3$, 400 MHz), δ (ppm): 7.49 (1H, C*H* triazole); 7.34–7.22 (5H, m, CH Ar,); 5.80 (1H, d, $J_{1,2}$ 9.3 Hz, H-1); 5.52 (1H, d, $J_{3,4}$ 3.5 Hz, H-4); 5.50 (1H, pseudo t, *J* 9.7 Hz, H-2); 5.22 (1H, dd, $J_{2,3}$ 10.2 Hz, $J_{3,4}$ 3.5 Hz, H-3); 4.21–4.10 (5H, m, H-6, H-6′, H-5, CH_2); 2.19, 2.03, 1.99, 1.87 (12H, 4s, 4 × CH_3). ^{13}C NMR ($CDCl_3$, 100 MHz), δ (ppm): 170.3, 170.0, 169.8, 169.0 (*C*OCH_3); 148.2 (C-quat); 138.6 (C-quat); 128.7, 128.6, 126.5 (CH Ar); 119.8 (*C*H triazole) 86.2 (C-1); 74.0 (C-5); 70.8 (C-3); 67.8 (C-2); 66.8 (C-4); 61.2 (C-6); 32.1 (*C*H_2); 20.7, 20.6, 20.4, 20.2 (CO*C*H_3). IR (KBr) ν_{max}: 1751.2;1369.4; 1220.9; 1064.6 cm^{-1}. ESI-MS *m*/*z*, calcd for $C_{23}H_{27}N_3O_9$ $[M+H]^+$ 490.1; $[M+Na]^+$ 512.1, found 490.0; 512.2. Deprotected compound **32d**: ESI-MS *m*/*z*, calcd for $C_{15}H_{19}N_3O_5$ $[M+Na]^+$ 344.1, found 344.2.

4.4.30. 2-[1-(β-D-Galactopyranosyl)-1*H*-1,2,3-triazol-4-yl]-phenylethane (33d)

Tetraacetate **33b**: (75% yield); ^{1}H NMR ($CDCl_3$, 400 MHz), δ (ppm): 7.49 (1H, C*H* triazole) 7.31–7.19 (5H, m, CH Ar,); 5.81 (1H, d, $J_{1,2}$ 9.3 Hz, H-1); 5.56–5.51 (2H, m, H-2, H-4); 5.23 (1H, dd, $J_{2,3}$ 10.3, $J_{3,4}$ 3.4 Hz, H-3); 4.22–4.11 (3H, m, H-6, H-6′, H-5) 3.07–2.98 (4H, m, CH_2); 2.21, 2.05, 2.01, 1.92 (12H, 4s, 4 × CH_3). ^{13}C NMR ($CDCl_3$, 100 MHz), δ (ppm): 170.3, 170.0, 169.8, 169.0 (*C*OCH_3); 148.0 (C-quat); 141.0 (C-quat); 128.4, 126.1 (CH Ar); 119.21 (*C*H triazole); 86.2 (C-1); 73.9 (C-5); 70.9 (C-3); 67.7 (C-2); 66.9 (C-4); 61.2 (C-6); 35.3 (*C*H_2); 27.5 (*C*H_2); 20.6, 20.5, 20.2 (CO*C*H_3). ESI-MS *m*/*z*, calcd for $C_{24}H_{29}N_3O_9$ $[M+H]^+$ 504.1; $[M+Na]^+$ 526.2, found 504.0; 526.2. Deprotected compound **33d**: ESI-MS *m*/*z*, calcd for $C_{16}H_{21}N_3O_5$ $[M+Na]^+$ 358.1, found 358.2.

4.4.31. 2-[1-(β-D-Galactopyranosyl)-1*H*-1,2,3-triazol-4-yl]-aniline (34d)

Tetraacetate **34b**: (88% yield); ^{1}H NMR ($CDCl_3$, 400 MHz), δ (ppm): 8.06 (1H, s, C*H* triazole); 7.42 (1H, d, $J_{3',4'}$ 7.5 Hz, H-3′); 7.12 (1H, t, *J* 8.4 Hz, H-5′); 6.76 (1H, m, H-4′, H-6′); 5.89 (1H, d, $J_{1,2}$ 9.3 Hz, H-1); 5.66 (1H, t, *J* 10.2 Hz, H-2); 5.57 (1H, d, $J_{4,5}$ 2.7 Hz, H-4); 5.32 (NH); 5.28 (1H, dd, $J_{2,3}$ 10.2 Hz, $J_{3,4}$ 3.4 Hz, H-3); 4.28–4.14 (3H, m, H-6, H-6′, H-5); 2.25, 2.05, 1.99, 1.89 (12H, 4s, 4 × CH_3). ^{13}C NMR ($CDCl_3$, 100 MHz), δ (ppm): 170.4, 170.0, 169.8, 169.1 (*C*OCH_3); 148.8 (C-quat triazole); 145.1 (C-2′); 129.4 (C-5′); 128.1 (C-3′); 118.3 (*C*H triazole); 117.5 (C-4′); 116.7 (C-6′); 113.2 (C-1′); 86.3 (C-1); 74.1 (C-5); 70.7 (C-3); 67.8 (C-2); 66.9 (C-4); 61.2 (C-6); 20.7, 20.6, 20.5, 20.2 (CO*C*H_3). ESI-MS *m*/*z*, calcd for $C_{22}H_{26}N_4O_9$ $[M+H]^+$ 491.1; $[M+Na]^+$ 513.1, found 491.0; 513.1. Deprotected compound **34d**: ESI-MS *m*/*z*, calcd for $C_{14}H_{18}N_4O_5$ $[M+H]^+$ 323.1; $[M+Na]^+$ 345.1, found 323.0; 345.1.

4.4.32. 2-[1-(β-D-Galactopyranosyl)-1*H*-1,2,3-triazol-4-yl]-bromobenzene (35d)

Tetraacetate **35b**: (93% yield); ^{1}H NMR ($CDCl_3$, 400 MHz), δ (ppm): 8.46 (1H, s, C*H* triazole); 8.05 (1H, dd, *J* 1.7 Hz, *J* 7.8 Hz, H-6′); 7.67 (1H, dd, *J* 1.2 Hz, *J* 8.0 Hz, H-3′); 7.59 (1H, d, *J* 8.0 Hz, H-4′); 7.42 (1H, dd, *J* 1.2 Hz, *J* 7.8 Hz, H-5′); 7.22 (1H, dt, *J* 1.7 Hz, *J* 1.2 Hz, *J* 8.0 Hz, CH Ar); 5.93 (1H, d, $J_{1,2}$ 9.5 Hz, H-1); 5.69 (1H, t, *J* 10.0 Hz, H-2); 5.58 (1H, d, $J_{3,4}$ 3.4 Hz, H-4); 5.29 (1H, dd, $J_{2,3}$ 10.3 Hz, $J_{3,4}$ 3.4 Hz, H-3); 4.28 (1H, dd, $J_{5,6}$ 5.8 Hz, $J_{5,6'}$ 6.9 Hz, H-5); 4.23 (1H, dd, $J_{5,6}$ 5.8 Hz, $J_{6,6'}$ 11.3 Hz, H-6); 4.17 (1H, dd, $J_{5,6'}$ 6.9 Hz, $J_{6,6'}$ 11.3 Hz H-6′); 2.24, 2.05, 2.02, 1.91 (12H, 4s, 4 × CH_3). ^{13}C NMR ($CDCl_3$, 100 MHz), δ (ppm): 170.3, 170.1, 169.8, 169.0 (*C*OCH_3); 146.0 (C-quat triazole); 133.6, 127.6 (C-quat Ar) 130.8, 129.7, (CH Ar); 121.4 (*C*H triazole); 86.3 (C-1); 74.1 (C-5); 70.9 (C-3); 67.7 (C-2); 66.9 (C-4); 61.2 (C-6); 20.7, 20.6, 20.5, 20.3 (CO*C*H_3). ESI-MS *m*/*z*, calcd for $C_{22}H_{24}BrN_3O_9$ $[M+Na]^+$ 575.8, found 576.0. Deprotected compound **35d**: ESI-MS *m*/*z*, calcd for $C_{14}H_{16}BrN_3O_5$ $[M+Na]^+$ 408.0, found 408.1.

4.4.33. 2-[1-(β-D-Galactopyranosyl)-1*H*-1,2,3-triazol-4-yl]-trifluoromethylbenzene (36d)

Tetraacetate **36b**: (100% yield); ^{1}H NMR ($CDCl_3$, 400 MHz), δ (ppm): 8.01 (1H, s, C*H* triazole); 7.88 (1H, d, *J* 7.8 Hz H-3′); 7.78 (1H, d, *J* 7.8 Hz, H-6′); 7.64 (1H, t, *J* 7.6 Hz, H-5′); 7.52 (1H, t, *J* 7.6 Hz, H-4′); 5.93 (1H, d, $J_{1,2}$ 9.3 Hz, H-1); 5.68 (1H, t, *J* 9.8 Hz, H-2); 5.58 (1H, d, $J_{3,4}$ 3.4 Hz, H-4); 5.29 (1H, dd, $J_{2,3}$ 10.2 Hz, $J_{3,4}$ 3.4 Hz, H-3); 4.27 (1H, pseudo t, *J* 6.4 Hz, H-5); 4.22 (1H, dd, $J_{5,6}$ 6.0 Hz, $J_{6,6'}$ 11.5 Hz, H-6); 4.18 (1H, dd, $J_{5,6'}$ 6.8 Hz, $J_{6,6'}$ 11.5 Hz, H-6′); 2.23, 2.04, 2.02, 1.91 (12H, 4s, 4 × CH_3). ^{13}C NMR ($CDCl_3$, 100 MHz), δ (ppm): 170.3, 170.1, 169.8, 168.9 (*C*OCH_3); 145.0 (C-quat triazole); 132.0, 128.9 (C-quat); 128.1, 127.5, 126.7 (CH Ar); 121.3 (*C*H triazole); 86.3 (C-1); 74.2 (C-5); 70.9 (C-3); 67.6 (C-2); 66.9 (C-4); 61.2 (C-6); 20.7, 20.6, 20.5, 20.1 (CO*C*H_3). ESI-MS *m*/*z*, calcd for $C_{23}H_{24}F_3N_3O_9$ $[M+Na]^+$ 566.1, found 566.1. Deprotected compound **36d**: ESI-MS *m*/*z*, calcd for $C_{15}H_{16}F_3N_3O_5$ $[M+Na]^+$ 398.1, found 398.1.

4.4.34. 4-[1-(β-D-Galactopyranosyl)-1*H*-1,2,3-triazol-4-yl]-aniline (37d)

Tetraacetate **37b**: (88% yield); ^{1}H NMR ($CDCl_3$, 400 MHz), δ (ppm): 7.91 (1H, s, C*H* triazole); 7.64 (2H, d, *J* 8.5 Hz, H-3′, H-5′); 7.29 (2H, d, *J* 8.5 Hz, H-2′, H-6′); 5.87 (1H, d, $J_{1,2}$ 9.5 Hz, H-1); 5.64 (1H, t, *J* 10.0 Hz, H-2); 5.56 (1H, d, $J_{3,4}$ 3.2 Hz, H-4); 5.26 (1H, dd, $J_{2,3}$ 10.0 Hz, $J_{3,4}$ 3.2 Hz, H-3); 4.24–4.13 (3H, m, H-6, H-6′, H-5); 3.82 (NH_2); 2.24, 2.06, 1.99, 1.89 (12H, 4s, 4 × CH_3). ^{13}C NMR ($CDCl_3$, 100 MHz), δ (ppm): 170.4, 170.1, 169.9, 169.2 (*C*OCH_3); 148.7 (C-4′); 147.0 (C-quat triazole); 127.1 (C-3′, C-5′); 120.4 (C-1′); 116.8 (C-2′, C6′); 115.2 (*C*H triazole); 86.3 (C-1); 74.1 (C-5); 70.8 (C-3); 68.1 (C-2); 67.1 (C-4); 61.4 (C-6); 20.8, 20.5, 20.3 (CO*C*H_3). ESI-MS *m*/*z*, calcd for $C_{22}H_{26}N_4O_9$ $[M+H]^+$ 491.1; $[M+Na]^+$ 513.1, found 491.1; 513.1. Deprotected compound **37d**: ESI-MS *m*/*z*, calcd for $C_{14}H_{18}N_4O_5$ $[M+H]^+$ 323.1; $[M+Na]^+$ 345.1, found 323.0; 345.1. ESI-HRMS $[M+Na]^+$ found 345.1168; calcd 345.1169.

4.4.35. 4-[1-(β-D-Galactopyranosyl)-1*H*-1,2,3-triazol-4-yl]-bromobenzene (38d)

Tetraacetate **38b**: (quantitative yield); ^{1}H NMR ($CDCl_3$, 400 MHz), δ (ppm): 8.06 (1H, s, C*H* triazole); 7.74 (2H, d, *J* 8.6 Hz, H-2′, H-6′); 7.57 (2H, d, *J* 8.6 Hz, H-3′, H-5′); 5.90 (1H, d, $J_{1,2}$ 9.3 Hz, H-1); 5.61 (1H, t, *J* 10 Hz, H-2); 5.58 (1H, dd, $J_{4,5}$ 1.0 Hz, $J_{3,4}$ 3.4 Hz, H-4); 5.29 (1H, dd, $J_{2,3}$ 10.2 Hz, $J_{3,4}$ 3.4 Hz, H-3); 4.27 (1H, t, *J* 6.4 Hz, H-5); 4.21 (1H, dd, $J_{5,6}$ 5.8 Hz, $J_{6,6'}$ 11.5 Hz, H-6); 4.17 (1H, dd, $J_{5,6'}$ 7.0 Hz, $J_{6,6'}$ 11.5 Hz, H-6′); 2.24, 2.04, 2.02, 1.90 (12H, 4s, 4 × CH_3). ^{13}C NMR ($CDCl_3$, 100 MHz), δ (ppm): 170.3, 170.0, 169.8, 169.2 (*C*OCH_3); 147.4 (C-quat triazole); 132.0, 127.4 (*C*H Ar), 128.9, 122.4 (C-quat Ar); 118.0 (*C*H triazole); 86.3 (C-1); 74.1 (C-5); 70.7 (C-3); 67.8 (C-2); 66.9 (C-4); 61.2 (C-6); 20.7, 20.6, 20.5, 20.3 (CO*C*H$_3$). ESI-MS *m*/*z*, calcd for $C_{22}H_{24}BrN_3O_9$ $[M+Na]^+$ 575.8, found 576.1. Deprotected compound **38d**: ESI-MS *m*/*z*, calcd for $C_{14}H_{16}BrN_3O_5$ $[M+HCOO]^-$ 430.0, found 429.9.

4.4.36. 4-[1-(β-D-Galactopyranosyl)-1*H*-1,2,3-triazol-4-yl]-trifluoromethylbenzene (39d)

Tetraacetate **39b**: (93% yield); ^{1}H NMR ($CDCl_3$, 400 MHz), δ (ppm): 8.18 (1H, s, C*H* triazole); 7.98 (2H, d, *J* 8.0 Hz, H-3′, H-5′); 7.69 (2H, d, *J* 8.3 Hz, H-2′, H-6′); 5.92 (1H, d, $J_{1,2}$ 9.3 Hz, H-1); 5.62 (1H, t, *J* 10.0 Hz, H-2); 5.59 (1H, d, $J_{3,4}$ 3.2 Hz, H-4); 5.29 (1H, dd, $J_{2,3}$ 10.2 Hz, $J_{3,4}$ 3.2 Hz, H-3); 4.28 (1H, t, *J* 6.4 Hz, H-5); 4.22 (1H, dd, $J_{5,6}$ 5.8 Hz, $J_{6,6'}$ 11.5 Hz, H-6); 4.12 (1H, dd,, $J_{5,6'}$ 7.1 Hz, $J_{6,6'}$ 11.5 Hz, H-6′); 2.25, 2.05, 2.03, 1.85 (12H, 4s, 4 × CH_3). ^{13}C NMR ($CDCl_3$, 100 MHz), δ (ppm): 170.3, 169.9, 169.8, 169.3 (*C*OCH_3); 147.1 (C-quat triazole); 133.4, 130.7 (C-quat Ar) 126.7, 126.0, (CH Ar); 118.8 (*C*H triazole); 86.4 (C-1); 74.2 (C-5); 70.7 (C-3); 67.8 (C-2); 66.9 (C-4); 61.2 (C-6); 20.7, 20.6, 20.5, 20.3 (CO*C*H$_3$). ESI-MS *m*/*z*, calcd for $C_{23}H_{24}F_3N_3O_9$ $[M+Na]^+$ 566.1, found 566.1. Deprotected compound **39d**: ESI-MS *m*/*z*, calcd for $C_{15}H_{16}F_3N_3O_5$ $[M+HCOO]^-$ 420.1, found 420.0.

4.4.37. 3-[1-(β-D-Galactopyranosyl)-1*H*-1,2,3-triazol-4-yl]-trifluoromethylbenzene (40d)

Tetraacetate **40b**: (100% yield); ^{1}H NMR ($CDCl_3$, 400 MHz), δ (ppm): 8.14 (1H, s, C*H* triazole); 8.11 (1H, s, H-2′); 8.07 (1H, d, *J* 7.6 Hz, H-6′); 7.58–7.43 (2H, m, H-4′, H-5′); 5.92 (1H, d, $J_{1,2}$ 9.3 Hz, H-1); 5.60 (1H, t, *J* 9.8 Hz, H-2); 5.59 (1H, d, $J_{3,4}$ 3.4 Hz, H-4); 5.30 (1H, dd, $J_{2,3}$ 10.3 Hz, $J_{3,4}$ 3.4 Hz, H-3); 4.28 (1H, pseudo t, *J* 6.4 Hz, H-5); 4.23 (1H, dd, $J_{5,6}$ 5.7 Hz, $J_{6,6'}$ 11.5 Hz, H-6); 4.19 (1H, dd, $J_{5,6'}$ 7.1 Hz, $J_{6,6'}$ 11.5 Hz, H-6′); 2.26, 2.05, 2.03, 1.92 (12H, 4s, 4 × CH_3). ^{13}C NMR ($CDCl_3$, 100 MHz), δ (ppm): 170.4, 170.0, 169.8, 169.2 (*C*OCH_3); 147.1 (C-quat triazole); 131.6, 130.8 (C-quat Ar); 126.6, 125.1, 124.8, 122.7 (CH Ar); 118.4 (*C*H triazole); 86.4 (C-1); 74.2 (C-5); 70.7 (C-3); 67.9 (C-2); 66.9 (C-4); 61.2 (C-6); 20.7, 20.6, 20.5, 20.3 (CO*C*H$_3$). ESI-MS *m*/*z*, calcd for $C_{23}H_{24}F_3N_3O_9$ $[M+Na]^+$ 566.1, found 566.1. Deprotected compound **40d**: ESI-MS *m*/*z*, calcd for $C_{15}H_{16}F_3N_3O_5$ $[M+Na]^+$ 398.1, found 398.1.

4.4.38. 2-[1-(β-D-Galactopyranosyl)-1*H*-1,2,3-triazol-4-yl]-*N*-phthalimidylmethane (41d)

Tetraacetate **41b**: (84% yield); ^{1}H NMR ($CDCl_3$, 400 MHz), δ (ppm): 7.93 (1H, s, C*H* triazole); 7.88–7.85 (2H, m, CH Ar); 7.76–7.71 (2H, m, CH Ar); 5.82 (1H, d, $J_{1,2}$ 9.5 Hz, H-1); 5.53 (1H, d, $J_{3,4}$ 3.4 Hz, H-4); 5.52 (1H, pseudo t, *J* 9.7 Hz, H-2); 5.23 (1H, dd, $J_{2,3}$ 10.3 Hz, $J_{3,4}$ 3.4 Hz, H-3); 5.05 (1H, d, *J* 15.4 Hz, CH_2); 4.96 (1H, d, *J* 15.4 Hz, CH_2); 4.23–4.16 (2H, m, H-6, H-6′); 4.09 (1H, q, $J_{5,6}$ 4.5, $J_{5,6'}$ 9.8 Hz, H-5); 2.24, 2.03, 1.99, 1.82 (12H, 4s, 4 × CH_3). ^{13}C NMR ($CDCl_3$, 100 MHz), δ (ppm): 170.3, 170.0, 169.8, 169.0 (*C*OCH_3); 167.6 (*C*O); 143.4 (C-quat triazole); 134.2, 132.0, 123.5 (C-quat, C*H* Ar); 121.5 (*C*H triazole); 86.2 (C-1); 74.1 (C-5); 70.8 (C-3); 67.8 (C-2); 66.9 (C-4); 61.2 (C-6); 32.9 (CH_2); 20.7, 20.6, 20.4, 20.2 (CO*C*H$_3$). ESI-MS *m*/*z*, calcd for $C_{25}H_{26}N_4O_{11}$ $[M+Na]^+$ 581.1, found 581.1. Deprotected compound **41d**: ESI-MS *m*/*z*, calcd for $C_{17}H_{18}N_4O_7$ $[M+Na]^+$ 413.1, found 413.1.

4.4.39. 2-[1-(β-D-Galactopyranosyl)-1*H*-1,2,3-triazol-4-yl]-pyridine (42d)

Tetraacetate **42b**: (95% yield); ^{1}H NMR ($CDCl_3$, 400 MHz), δ (ppm): 8.61 (1H, d, $J_{4',5'}$ 4.1 Hz, H-6′); 8.50 (1H, C*H* triazole) 8.16 (1H, d, $J_{2',3'}$ 8.0 Hz, H-3′); 7.79 (1H, dt, $J_{2',3'}$ 8.0 Hz, $J_{3',4'}$ 1.7 Hz, H-4′); 7.25 (1H, m, H-5′); 5.92 (1H, d, $J_{1,2}$ 9.2 Hz, H-1); 5.62 (1H, dd, $J_{1,2}$ 9.2 Hz, $J_{2,3}$ 10.2 Hz, H-2); 5.57 (1H, d, $J_{3,4}$ 3.4 Hz, H-4); 5.29 (1H, dd, $J_{2,3}$ 10.2 Hz, $J_{3,4}$ 3.4 Hz, H-3); 4.28 (1H, t, $J_{5,6}$ 5.8 Hz, $J_{5,6'}$ 6.8 Hz, H-5); 4.21 (1H, dd, $J_{5,6}$ 5.8 Hz, $J_{6,6'}$ 11.5 Hz, H-6); 4.15 (1H, dd, $J_{5,6'}$ 6.8 Hz, $J_{6,6'}$ 11.5 Hz, H-6′); 2.24, 2.04, 2.02, 1.92 (12H, 4s, 4 × CH_3). ^{13}C NMR ($CDCl_3$, 100 MHz), δ (ppm): 170.3, 170.0, 169.8, 169.0 (*C*OCH_3); 149.7 (C-2′); 149.5 (C-6′); 148.9 (C-quat triazole); 136.9 (C-4′), 123.1 (C-5′), 120.6 (C-3′); 120.3 (*C*H triazole); 86.3 (C-1); 74.0 (C-5); 70.8 (C-3); 68.0 (C-2); 66.9 (C-4); 61.3 (C-6); 20.7, 20.6, 20.5, 20.3 (CO*C*H$_3$). ESI-MS *m*/*z*, calcd for $C_{21}H_{24}N_4O_9$ $[M+H]^+$ 477.1; $[M+Na]^+$ 499.0, found 477.0; 499.1. Deprotected compound **42d**: ESI-MS *m*/*z*, calcd for $C_{13}H_{16}N_4O_5$ $[M+Na]^+$ 331.1, found 331.1.

4.4.40. 3-[1-(β-D-Galactopyranosyl)-1*H*-1,2,3-triazol-4-yl]-pyridine (43d)

Tetraacetate **43b**: (quantitative yield); ^{1}H NMR ($CDCl_3$, 400 MHz), δ (ppm): 9.06 (1H, br s, H-2′); 8.61 (1H, br s, H-6′); 8.22 (1H, dd, $J_{4',5'}$ 7.8 Hz, $J_{4',6'}$ 1.7 Hz, H-4′); 8.17 (C*H* triazole); 7.39 (1H, dd, $J_{4',5'}$ 7.8 Hz, $J_{5',6'}$ 4.8 Hz, H-5 ′); 5.94 (1H, d, $J_{1,2}$ 9.3 Hz, H-1); 5.63 (1H, pseudo t, *J* 9.8 Hz, H-2); 5.59 (1H, dd, $J_{3,4}$ 3.4 Hz, $J_{4,5}$ 1.0 Hz, H-4); 5.30 (1H, d, $J_{2,3}$ 10.3 Hz, $J_{3,4}$ 3.4 Hz, H-3); 4.30 (1H, dd, $J_{4,5}$ 1.0 Hz, $J_{5,6}$ 5.8 Hz, $J_{5,6'}$ 7.0 Hz, H-5); 4.23 (1H, dd, $J_{5,6}$ 5.8 Hz, $J_{6,6'}$ 11.4 Hz, H-6); 4.19 (1H, dd, $J_{5,6'}$ 7.0 Hz, $J_{6,6'}$ 11.4 Hz, H-6′); 2.27, 2.05, 2.03, 1.92 (12H, 4s, 4 × CH_3). ^{13}C NMR ($CDCl_3$, 100 MHz), δ (ppm): 170.3, 170.0, 169.8, 169.2 (*C*OCH_3); 149.6 (C-6′) 147.2 (C-2′); 145.4 (C-quat); 133.1 (C-4′); 126.2 (C-3′); 123.7 (C-5′); 118.4 (*C*H triazole); 86.4 (C-1); 74.2 (C-5); 70.7 (C-3); 67.9 (C-2); 66.9 (C-4); 61.2 (C-6); 20.7, 20.6, 20.5, 20.2 (CO*C*H$_3$). IR (KBr) ν_{max}: 1753.2; 1369.4; 1222.8; 1064.6 cm^{-1}. ESI-MS *m*/*z*, calcd for $C_{21}H_{24}N_4O_9$ $[M+H]^+$ 477.1; $[M+Na]^+$ 499.0, found 477.0; 499.1. Deprotected compound **43d**: ESI-MS *m*/*z*, calcd for $C_{13}H_{16}N_4O_5$ $[M+HCOO]^-$ 353.1, found 352.9.

4.4.41. *N*-Benzyl-*N*-methyl-1-[1-(β-D-galactopyranosyl)-1*H*-1,2,3-triazol-4-yl]-methylamine (44d)

Tetraacetate **44b**: (84% yield); ^{1}H NMR ($CDCl_3$, 400 MHz), δ (ppm): 7.79 (1H, s, C*H* triazole); 7.37–7.24 (5H, m, CH Ar); 5.84 (1H. d. $J_{1,2}$ 9.3 Hz, H-1); 5.55 (2H, dd, $J_{1,2}$ 9.3 Hz, $J_{2,3}$ 10.4 Hz, H-2, H-4); 5.25 (1H, dd, $J_{2,3}$ 10.4 Hz, $J_{3,4}$ 3.4 Hz, H-3); 4.23 (1H, pseudo t, *J* 6.2 Hz, H-5); 4.20 (1H, dd, $J_{5,6}$ 5.9 Hz, $J_{6,6'}$ 11.1 Hz, H-6); 4.15 (1H, dd, $J_{5,6'}$ 6.7 Hz, $J_{6,6'}$ 11.1 Hz, H-6′); 3.75 (1H, d, *J* 14.1 Hz, CH_2); 3.72 (1H, d, *J* 14.1 Hz, CH_2); 3.57 (1H, d, *J* 13.3 Hz, CH_2); 3.52 (1H, d, *J* 13.3 Hz, CH_2); 2.23, 2.04, 2.01, 1.85 (15H, 5s, 5 × CH_3). ^{13}C NMR ($CDCl_3$, 100 MHz), δ (ppm): 170.3, 170.0, 169.8, 169.0 (*C*OCH_3); 146.0 (C-quat triazole); 138.5 (C-quat Ar); 129.1, 128.2, 127.2 (*C*H Ar); 121.0 (*C*H triazole); 86.3 (C-1); 74.0 (C-5); 70.8 (C-3); 67.9 (C-2); 66.9 (C-4); 61.3 (C-6); 61.2 (*C*H_2); 51.9 (*C*H_2); 41.9 (N*C*H$_3$); 20.7, 20.6, 20.5, 20.2 (CO*C*H$_3$). ESI-MS *m*/*z*, calcd for $C_{25}H_{32}N_4O_9$ $[M+H]^+$ 533.2; $[M+Na]^+$ 555.2, found 533.1; 555.1. Deprotected compound **44d**: ESI-MS *m*/*z*, calcd for $C_{17}H_{24}N_4O_5$ $[M+H]^+$ 365.1; $[M+Na]^+$ 387.1, found 365.1; 387.2.

4.4.42. 4-[1-(β-D-Galactopyranosyl)-1*H*-1,2,3-triazol-4-yl]-butanoic acid (45d)

Tetraacetate **45b**: (81% yield); ^{1}H NMR ($CDCl_3$, 400 MHz), δ (ppm): 7.64 (1H, s, C*H* triazole); 5.83 (1H, d, $J_{1,2}$ 9.3 Hz, H-1); 5.56–5.51 (2H, m, H-2, H-4); 5.25 (1H, dd, $J_{2,3}$ 10.2 Hz, $J_{3,4}$ 3.4 Hz,

H-3); 4.24–4.20 (2H, m, H-6, H-5); 4.15 (1H, dd, $J_{5,6'}$ 6.8 Hz, $J_{6,6'}$ 11.0 Hz, H-6′); 2.82 (2H, dt, *J* 2.8 Hz, *J* 7.3 Hz, CH_2); 2.42 (2H, t, *J* 7.3 Hz, CH_2); 2.23 (3H, s, CH_3); 2.05–2.01 (8H, 2s, m, 2 × CH_3, CH_2); 1.89 (3H, s, CH_3). ^{13}C NMR ($CDCl_3$, 100 MHz), δ (ppm): 178.2 (CO_2H); 170.4, 170.0, 169.9, 169.2 (COCH_3); 147.7 (C-quat triazole); 119.5 (*C*H triazole); 86.3 (C-1); 74.0 (C-5); 70.8 (C-3); 67.9 (C-2); 66.9 (C-4); 61.2 (C-6); 32.9 (CH_2); 24.6 (CH_2); 24.1 (CH_2); 20.7, 20.5, 20.3 (COCH_3). IR (KBr) ν_{max}: 2939.3; 1751.2; 1220.9; 1062.7 cm^{-1}. ESI-MS *m*/*z*, calcd for $C_{20}H_{27}N_3O_{11}$ [M+H]$^+$ 486.1; [M+Na]$^+$ 508.1, found 486.0; 508.2. Deprotected compound **45d**: ESI-MS *m*/*z*, calcd for $C_{12}H_{19}N_3O_7$ [M+Na]$^+$ 340.1; [M+2Na]$^+$ 363.0, found 340.2 363.2.

4.4.43. (2*R*/*S*)-1-[1-(β-D-Galactopyranosyl)-1*H*-1,2,3-triazol-4-yl]-propan-2-ol (46d)

Tetraacetate **46b**: (87% yield); ^{1}H NMR ($CDCl_3$, 400 MHz), δ (ppm): 7.73 (1H, s, C*H* triazole); 5.83, 5.81 (1H, 2 × d, $J_{1,2}$ 9.3 Hz, H-1); 5.56 (1H, d, $J_{3,4}$ 3.2 Hz, H-4); 5.46 (1H, dt, $J_{1,2}$ 9.3 Hz, $J_{2,3}$ 10.2 Hz, H-2); 5.27 (1H, dd, $J_{2,3}$ 10.2 Hz, $J_{3,4}$ 3.2 Hz, H-3); 4.25–4.15 (4H, m, H-6, H-6′, H-5, C*H*OH); 2.93–2.70 (2H, m, CH_2); 2.22, 2.05, 2.01, 1.89 (12H, 4s, 4 × CH_3); 1.29–1.25 (3H, m, CH_3). ^{13}C NMR ($CDCl_3$, 100 MHz), δ (ppm): 170.3, 170.0, 169.8, 169.3 (COCH_3); 146.0, 145.7 (C-quat triazole); 120.8, 120.5 (*C*H triazole); 86.3 (C-1); 74.0 (C-5); 70.7, 70.6 (C-3); 68.2, 68.0 (C-2); 67.1 (*C*HOH); 66.9, 66.8 (C-4); 61.2 (C-6); 35.2, 34.8 (CH_2); 22.7 (CH_3); 20.7, 20.6, 20.5, 20.2 (COCH_3). ESI-MS *m*/*z*, calcd for $C_{19}H_{27}N_3O_{10}$ [M+H]$^+$ 458.1; [M+Na]$^+$ 480.1, found 458.0; 480.1. Deprotected compound **46d**: ESI-MS *m*/*z*, calcd for $C_{11}H_{19}N_3O_6$ [M+Na]$^+$ 312.1, found 312.2.

4.4.44. (1*R*/*S*)-1-[1-(β-D-Galactopyranosyl)-1*H*-1,2,3-triazol-4-yl]-propan-1-ol (47d)

Tetraacetate **47b**: (100% yield); ^{1}H NMR ($CDCl_3$, 400 MHz), δ (ppm): 7.79, 7.78 (1H, s, CH triazole); 5.85 (1H, d, $J_{1,2}$ 9.3 Hz, H-1); 5.57–5.51 (2H, m, H-4, H-2); 5.26 (1H, dd, $J_{2,3}$ 10.2 Hz, $J_{3,4}$ 3.4 Hz, H-3); 4.85 (1H, m, C*H*OH); 4.24 (1H, t, *J* 6.6 Hz, H-5) 4.22–4.13 (2H, m, H-6, H-6′); 2.70, 2.65 (1H, 2 × s, OH); 2.23, 2.05, 2.04, 1.88 (12H, 4s, 4 × CH_3, CH_2); 1.93–1.86 (2H, m, CH_2); 0.98 (3H, t, *J* 7.3 Hz, CH_3). ^{13}C NMR ($CDCl_3$, 100 MHz), δ (ppm): 170.4, 170.0, 169.8, 169.1 (COCH_3); 152.0 (C-quat triazole); 119.1 (*C*H triazole); 86.2 (C-1); 74.0 (C-5); 70.7 (C-3); 68.3 (*C*HOH); 67.9 (C-2); 66.9 (C-4); 61.2 (C-6); 30.3 (CH_2);. 20.7, 20.6, 20.5, 20.2 (COCH_3); 9.5 (CH_3). ESI-MS *m*/*z*, calcd for $C_{19}H_{27}N_3O_{10}$ [M+H]$^+$ 458.1; [M+Na]$^+$ 480.1, found 458.0; 480.1. Deprotected compound **47d**: ESI-MS *m*/*z*, calcd for $C_{11}H_{19}N_3O_6$ [M+Na]$^+$ 312.1, found 312.1.

4.4.45. 1,3-Bis{1-[(β-D-galactopyranosyl)]-1*H*-1,2,3-triazol-6-yl}-propane (48d)

Tetraacetate **48b**: (44% yield); ^{1}H NMR ($CDCl_3$, 400 MHz), δ (ppm): 7.65 (2H, s, C*H* triazole); 5.82 (2H, d, $J_{1,2}$ 9.2 Hz, H-1); 5.59–5.52 (4H, m, H-4, H-2); 5.24 (2H, dd, $J_{2,3}$ 10.2 Hz, $J_{3,4}$ 3.4 Hz, H-3); 4.24–4.12 (6H, m, H-6, H-6′, H-5); 2.78 (4H, dt, *J* 2.9 Hz, *J* 7.3 Hz, CH_2); 2.23, 2.05, 2.01, 1.89 (24H, 4s, 4 × CH_3); 2.12–2.05 (2H, m, CH_2). ^{13}C NMR ($CDCl_3$, 100 MHz), δ (ppm): 170.4, 170.0, 169.8, 169.1 (COCH_3); 148.1 (C-quat triazole); 119.4 (*C*H triazole); 86.2 (C-1); 74.0 (C-5); 70.8 (C-3); 67.8 (C-2); 66.9 (C-4); 61.2 (C-6); 28.5 (CH_2); 24.8 (CH_2); 20.7, 20.5, 20.3 (COCH_3). ESI-MS *m*/*z*, calcd for $C_{35}H_{46}N_6O_{18}$ [M+H]$^+$ 839.3; [M+Na]$^+$ 861.3, found 839.4; 861.3. Deprotected compound **48d**: ESI-MS *m*/*z*, calcd for $C_{19}H_{30}N_6O_{10}$ [M+Na]$^+$ 525.2, found 525.3. ESI-HRMS [M+H]$^+$ found 503.2096; calcd 503.2096.

4.4.46. Methyl [1-(β-D-galactopyranosyl)-1*H*-1,2,3-triazol-4-yl]-carboxylate (49d)

Tetraacetate **49b**: (96% yield); ^{1}H NMR ($CDCl_3$, 400 MHz), δ (ppm): 8.41 (1H, s, C*H* triazole); 5.90 (1H, dd, $J_{1,2}$ 9.3 Hz, H-1); 5.57 (1H, d, $J_{3,4}$ 3.2 Hz, H-4); 5.50 (1H, pseudo t, *J* 9.7 Hz, H-2); 5.28 (1H, dd, $J_{2,3}$ 10.2 Hz, $J_{3,4}$ 3.2 Hz, H-3); 4.26 (1H, pseudo t, *J* 6.3 Hz, H-5); 4.21 (1H, dd, $J_{5,6}$ 5.8 Hz, $J_{6,6'}$ 11.5 Hz, H-6); 4.16 (1H, dd, $J_{5,6'}$ 7.0 Hz, $J_{6,6'}$ 11.5 Hz, H-6′); 3.98 (3H, s, CO_2CH3); 2.23, 2.05, 1.99, 1.89 (12H, 4s, 4 × CH_3). ^{13}C NMR ($CDCl_3$, 100 MHz), δ (ppm): 170.3, 169.9, 169.8, 169.2 (COCH_3); 160.7 (CO_2CH_3); 140.6 (C-quat triazole); 126.3 (CH triazole); 86.5 (C-1); 74.3 (C-5); 70.5 (C-3); 68.0 (C-2); 66.8 (C-4); 61.2 (C-6); 52.4 (CO_2CH3); 20.6, 20.5, 20.2 (COCH_3). IR (KBr) ν_{max}: 1751.2; 1369.4; 1218.9; 1064.6 cm^{-1}. ESI-MS *m*/*z*, calcd for $C_{18}H_{23}N_3O_{11}$ [M+Na]$^+$ 480.1, found 480.1. Deprotected compound **49d**: ESI-MS *m*/*z*, calcd for $C_{10}H_{15}N_3O_7$ [M+Na]$^+$ 312.1, found 312.1.

4.4.47. [1-(β-D-Galactopyranosyl)-1*H*-1,2,3-triazol-4-yl]-methanol *O*-(*R*/*S*)-epoxypropyl ether (50d)

Tetraacetate **50b**: (88% yield); ^{1}H NMR ($CDCl_3$, 400 MHz), δ (ppm): 7.88 (1H, s, C*H* triazole); 5.85 (1H, d, $J_{1,2}$ 9.3 Hz, H-1); 5.54 (1H, t, *J* 9.7 Hz, H-2); 5.53 (1H, d, $J_{3,4}$ 3.4 Hz, H-4); 5.25 (1H, dd, $J_{2,3}$ 10.5 Hz, $J_{3,4}$ 3.4 Hz, H-3); 4.75 (1H, d, *J* 12.4 Hz, CH_2); 4.70 (1H, d, *J* 12.4 Hz, CH_2); 4.24 (1H, pseudo t, *J* 6.3 Hz, H-5); 4.18 (1H, dd, $J_{5,6}$ 5.6 Hz, $J_{6,6'}$ 11.4 Hz, H-6); 4.14 (1H, dd, $J_{5,6'}$ 7.0 Hz, $J_{6,6'}$ 11.4 Hz, H-6′); 3.83 (1H, ddd, *J* 3.0 Hz, *J* 5.8 Hz, CH_2); 3.45 (1H, q, *J* 5.8 Hz, CH_2); 3.20 (1H, sl, C*H*); 2.81 (1H, t, *J* 4.6 Hz, CH_2); 2.64 (1H, dd, *J* 3.0 Hz, *J* 4.6 Hz, CH_2); 2.23, 2.05, 2.01, 1.90 (12H, 4s, 4 × CH_3). ^{13}C NMR ($CDCl_3$, 100 MHz), δ (ppm): 170.4, 170.0, 169.8, 169.1 (COCH_3); 145.6 (C-quat triazole); 121.2 (*C*H triazole); 86.3 (C-1); 74.0 (C-5); 71.1 (CH_2); 70.8 (C-3); 67.9 (C-2); 66.9 (C-4); 64.5 (CH_2); 61.2 (C-6); 50.6 (CH); 44.3 (CH_2); 20.7, 20.6, 20.5, 20.3 (COCH_3). IR (KBr) ν_{max}: 1753.2; 1371.3; 1220.9; 1064.6 cm^{-1}. ESI-MS *m*/*z*, calcd for $C_{20}H_{27}N_3O_{11}$ [M+H]$^+$ 486.1, found 486.2. Deprotected compound **50d**: ESI-MS *m*/*z*, calcd For $C_{12}H_{19}N_3O_7$ [M+H]$^+$ 318.1, found 318.1.

4.5. Biological assays

4.5.1. Fluorimetric TcTS inhibition assay

trans-Sialidase used in this study was a His-tagged 70 kDa recombinant material truncated to remove C-terminal repeats but retaining the catalytic N-terminal domain of the enzyme.[43] Inhibition was assessed using the continuous fluorimetric assay described by Douglas and co-workers.[40e] Briefly, the assay was performed in duplicate in 96-well plates containing phosphate buffer solution at pH 7.4 (25 μL), recombinant enzyme solution (25 μL) and inhibitor solution (25 μL of a 4.0 mM solution). This mixture was incubated for 10 min at 26 °C followed by addition of MuNANA (K_m = 0.68 mM;[40e] 25 μL of a 0.4 mM solution giving an assay concentration of 0.1 mM). The fluorescence of the released product (Mu) was measured after 10 min, with excitation and emission wavelengths of 360 and 460 nm, respectively, and the data were analyzed with GraphPad Prism software version 4.0 (San Diego, CA, USA). Inhibition percentages were calculated by the equation: % $I = 100 \times [1 - (V_i/V_0)]$, where V_i is the velocity in the presence of inhibitor and V_0 is the velocity in absence of inhibitor.

4.5.2. Sialic acid transfer reactions catalyzed by TcTS

A cell free extract containing TcTS was obtained from a cell pellet of the expression strain, which was thawed on ice and re-suspended in 30 ml of phosphate buffer saline (PBS). After 30 min incubation on ice, the viscosity of the solution was decreased by addition of DNase (20 μg/mL). The cells were then sonicated on ice for 5 × 1 min cycles, with 1 min intervals between bursts. The suspension was centrifuged to remove cell debris and the supernatant was filtered through a 0.22 μm filter. The cleared protein lysate obtained was employed without further purification in biotransformations.

The enzymatic reactions were conducted with 2′-(4-methylumbelliferyl)-α-D-*N*-acetylneuraminic acid (sodium salt) as a donor

substrate. To a solution of donor substrate (20 μL of a 5 mM in 0.1 M phosphate buffer pH 7.5, 5 equiv) and acceptor substrate (20 μL of a 1 mM solution in 0.1 M phosphate buffer pH 7.5, 1 equiv) was added 10 μL of the crude TcTS to effect complete conversion within 4 h at 25–30 °C. After completion of the reaction, as judged by TLC (CH_3CN/EtOAc/Isopropanol/H_2O, 85:20:50:3, v/v), protein was precipitated by addition of EtOH (50 μL) and the mixture was then centrifuged. The supernatant was transferred to a new Eppendorf tube and analyzed by mass spectrometry. TLC plates were visualized by dipping into orcinol solution and heating. The release of umbelliferone from the donor was observed by UV lamp only, which showed the donor as small bright spot at low R_f and the by-product umbelliferone as a much brighter spot at higher R_f (CH_3CN/EtOAc/Isopropanol/H_2O, 85:20:50:3, v/v). Lactose and methyl β-D-galactopyranoside were used as positive controls in parallel biotransformation reactions. Control reactions were also carried out in the presence of the donor and enzyme without acceptor. Generally, acceptor compounds were dissolved in H_2O to give a 10 mM stock solution, which was diluted 10-fold with 0.1 M phosphate buffer 7.5 prior to use. However, compounds **38a**, **38b**, **39a**, **39b**, **41a** and **43b** were only soluble in water to a limited extent, with **41a** being the least soluble one. These compounds were dissolved at 1 mM concentration in a buffer pH 7.5 containing 0.6% v/v of DMSO. As reported by Schrader et al.[40c] 0.6% v/v DMSO does not interfere with the TcTS activity.

4.5.3. In vitro evaluation of the trypanocidal activity

In vitro trypanocidal activity of the triazole-galactoside library **28–50** (**c** and **d** series) was evaluated against trypomastigote forms of *T. cruzi* Y strain obtained from a cultured cell line (LLC-MK_2).[46] Trypomastigote cultures were re-suspended at 6.5×10^6 parasites/ml in RPMI (Roswell Park Memorial Institute) containing 10% fetal bovine serum (FBS). Three independent experiments were performed for each product at five concentrations (1000, 750, 500, 250 and 100 μM), at 37 °C, 5% CO_2. Benznidazole (*N*-benzyl-2-nitro-1-imidazolacetamide) (same concentrations as above) was used as a reference trypanocidal drug (positive control). Parasite viability was subsequently determined by counting the number of motile forms after 24 h, as described by Brener.[47]

4.5.4. Cytotoxicity assay

Mammalian cell cytoxicity was evaluated using the protocol reported by Silva et al.[48] Spleen cells from C57BL/6 mice were isolated by mechanical dissociation, followed by incubation for 4 min with red blood cell lysis buffer (one part of 0.17 M Tris–HCl [pH 7.5] and nine parts of 0.16 M ammonium chloride). The cells were washed and suspended in RPMI 1640 (Gibco-BRL Life Technologies, Grand Island, NY) supplemented with 5% fetal calf serum (Life Technologies Inc., Bethesda, MD), 50 μM β-mercaptoethanol, 2 mM L-glutamine and antibiotics (all purchased from Sigma Chemical Co., St. Louis). The cell suspension was cultured in flat-bottom 96-well plates at 5×10^5 cells per well with different concentrations of the test compounds (series **c** and **d**) and incubated at 37 °C in a humidified atmosphere of 5% CO_2 for 24 h. Tween 20 at 0.5% was used as cell death positive control. To analyze cytotoxicity, cells were harvested, incubated with 10 μg/mL propidium iodide (Sigma Chemical Co., St. Louis) and after 15 min data were acquired using a FACSCantoII (Becton-Dickinson Immunocytometry System Inc., San Jose, CA, USA). Data analysis was performed using FlowJo software (Ashland, Oregon, USA).

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Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.bmc.2010.02.053.

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